Institution: University of Salford

Unit of Assessment: C17 Geography, Environmental Studies and Archaeology

Title of case study: Landscape controls on the transmission of fatal human infection

1. Summary of the impact

Geographical research at the University of Salford over the last 12 years has developed understanding of the effects of landscape structure and landscape change, on the transmission of a fatal parasitic tapeworm infection in humans. As a result of this, and related research:

- Parasite control programmes have been introduced in western China and Kyrgyzstan;
- The risk of parasite transmission to humans has been reduced;
- Reductions in human mortality are expected.

2. Underpinning research

The key researchers and positions they held at the institution at the time of the research are as follows: Professor Mark Danson, Professor of Environmental Remote Sensing (from 1990), Dr Richard Armitage, Lecturer in GIS (from 1998) and Professor Philip Craig, Professor of Parasitology (from 1992 - submitted to UoA5). **Context:** Human infection with the larval stage of the fox tapeworm *Echinococcus multilocularis* (Em), widely regarded as one of the world's most dangerous parasites, causes death in over 90% of infected patients. Transmission of the parasite to humans causes the hydatid disease human Alveolar Echinococcosis (AE), a degenerative liver infection, which requires specific environmental and socio-ecological conditions that are found across much of the northern hemisphere. The definitive hosts of the parasite include the geographically widely distributed red fox, corsac fox, Tibetan fox and wolf, and the intermediate hosts of the tapeworm include a wide range of small mammal species associated with temperate grasslands, for example the plateau pika (*Ochotona*) in western China and Tibet.

- **2000-2004:** Before 2000 the spatial distribution of human AE was known only at very coarse spatial scales, based on sporadic and often unverified hospital records showing that the disease was present across broad regions of western China, central Asia, Europe and North America. Working with experts in the parasitology and epidemiology of Em transmission at the University of Salford (Professor Philip Craig - submitted to UoA5), and with support from the US National Institutes of Health (NIH) **[10]**, Danson et al. **[6]** were the first to show that the spatial distribution of human AE in counties across China correlated with the spatial distribution of temperate grasslands, defined from the International Geosphere Biosphere Programme (IGBP) global land cover classification, confirming a hypothesised link between disease transmission and landscape. **[4]**
- Following a study to determine Human AE prevalence in 31 villages in south Gansu Province, China, Danson et al. (2004) showed that landscape composition around the villages, derived from archived Landsat imagery, was significantly correlated with village level prevalence of the disease, highlighting the patchy, local scale of transmission of the parasite to humans. This link provided further evidence to support the hypothesis that free-roaming domestic dogs, preying on infected small mammals around villages, may become infected with EM and be responsible for a 'peri-domestic' cycle where the parasite is introduced into the human environment through eggs shed in domestic dog faeces. **[5]**

- **2005-2008:** With further support from the US National Institutes of Health and National Science Foundation **[8]**, this work was extended to the eastern Tibetan plateau where AE prevalence in nomadic yak herders was found to be high. Extensive surveys of the domestic dog population, led by Craig, showed infection rates of up to 25% with widespread environmental contamination with tapeworm eggs in and around villages and nomadic camps. Danson and Armitage worked with small mammal ecologist Professor Patrick Giraudoux and colleagues at the University of Franche Comté, France, to examine the relationships between landscape and the distribution of EM-susceptible small mammal communities, identifying Ochotona and Microtus species as likely intermediate hosts and

mapping transmission risk using Landsat and Modis Terra data. **[2,4]**. Further evidence of the link between landscape and human AE was provided through work in Ningxia Province, China, including a predictive model of AE across an agricultural landscape with active EM transmission. **[1,3]** and in Kazakhstan in pastoralist communities. **[9]**

- In **2011** a Welcome Trust grant was awarded to Salford (Craig PI, Danson CoPI) to extend the work on the Tibetan plateau and central Asia to implement and test a parasite control programme through the application of anti-helminthics (to kill the tapeworm) to large populations of domestic dogs. The first fieldwork in the Osh oblast of southern Kyrgyzstan in May 2012 confirmed an emerging hyper-endemic focus of Em in dogs and small mammals, and an emerging health crisis in the human population with large numbers of AE cases being diagnosed. **[7]**

3. References to the research

Key outputs

1. Pleydell, D.R.J., Yang, Y., Danson, F.M., Raoul, F., Craig, P.S., McManus, D.A., Vuitton, D.A., Wang, Q., & Giraudoux, P., 2008, *Landscape composition and spatial prediction of alveolar echinococcosis in southern Ningxia, china*, PLoS Neglected Tropical diseases. 2(9): e287. DOI **(REF 2)**
2. Danson, F.M., Armitage, R.P., & Marston, C.G., 2008, *Spatial and temporal modelling for parasite transmission studies and risk assessment*. Parasite, 15(3) 463-468. DOI
3. Yang, Y.R., Sun, T., Li, Z.Z., Zhang, J.Z., Teng, J., Liu, X.Z., Liu, R.Q., Zhao, R., Jones, M.K., Wang, Y.H., Wen, H., Feng, X.H., Zhao, Q., Zhao, Y.M., Shi, D.Z., Bartholomot, B., Vuitton, D.A., Pleydell, D.R.J., Giraudoux, P., Ito, A., Danson, F.M., Boufana, B., Craig, P.S., Williams, G.M. & McManus, D.P., 2006, *Community surveys and risk factor analysis of human alveolar and cystic echinococcosis in Ningxia Hui Autonomous Region, China* , Bulletin of the World Health Organization, 84 (9) , pp. 714-721. DOI
4. Danson, F.M., Giraudoux, P., & Craig, P.S, 2006. *Spatial modelling and ecology of Echinococcus multilocularis transmission in China.* Parasitology International, 55, S227-S231. URL
5. Danson, F.M, Craig, P.S., Man, W., 2004. *Landscape dynamics and risk modelling of human alveolar echinococcosis*. Photogrammetric Engineering and Remote Sensing, 70(3), 359-366. URL
6. Danson, F.M., Graham, A.J., Pleydell, D.R.J., Campos-Ponce, M, Giraudoux, P., & Craig, P.S., 2003. *Multi-scale spatial analysis of human alveolar echinococcosis risk in China*. Parasitology, 127, S133-S141. DOI

Key grants

7. **2011:** Multi-species transmission of Echinococcus on the Tibetan plateau, Wellcome Trust, £733,851, Danson Co-PI 20%
8. **2005:** Ecosystem disturbance and multiscale transmission of zoonotic wildlife pathogen, US National Institutes of Health, £349,160, Danson Co-PI 40%
9. **2004:** Ecology of EM and Transmission to Humans in Kazakhstan and Kyrgyzstan, European Union, £5,054, Danson PI 100%
10. **2000:** Parasitic zoonosis (echinococcosis) transmission in China, US National Institutes of Health, £465,532.00, Danson (Co-PI) 25%
11. **2001:** Risk Assessment and Prevention of Alveolar Echinococcosis (ECHINORISK), European Union £21,724, Danson (PI) 50%

4. Details of the impact

Danson et al provided the first clear evidence that landscape change affects the spatial distribution of the Em parasite, and that the spatial organisation of landscape elements, including parasite host habitat, dogs, and human populations, creates local-scale patchiness to transmission risk. This understanding has impacted directly on disease prevention, and control of the parasite, which the World Health Organization notes, *"…are perhaps some of the more important global parasitic diseases, with more than 1 million people affected at any one time, many showing severe clinical syndromes."* **[a]**

- The key impact of the work is the understanding that the local-scale spatial arrangement of landscape around human settlements has a direct effect on the risk of transmission to individuals and communities, enabling the development of key public health messages to individuals and communities in the endemic areas, that "*proximity to habitat that supports the intermediate hosts of the parasite, and the accessibility of free-ranging domestic dogs to this habitat directly affects the likelihood of infection with the parasite*." Danson et al have carried out targeted surveys in numerous remote communities in western China, Kazakhstan and Kyrgyzstan, as well as European hotspots in eastern France, southern Germany and Switzerland **[11]**, raising awareness of disease transmission mechanisms, and prevention, for more than 10,000 people.

- The success of this research, and its subsequent impact, is a result of cross-disciplinary working, international collaboration, and close involvement in the fieldwork of medical teams and government organisations responsible for human health in the endemic areas. Impact is demonstrated not only on the health and well-being of individuals in the endemic areas, but also through an emerging focus on better understanding the spatial nature of the risk factors for human AE, and the design of disease control strategies, in organisations responsible for in-country health management.

- In the work described the unique and critical contribution of Danson's work is the explicit integration of spatial sampling and spatial mapping and modelling techniques. In contrast to earlier epidemiological surveys undertaken in Asia, north America and Europe, current survey methods adopted by agencies like the Sichuan Centre for Diseases Control and Prevention (China) now include, as a direct result of the work undertaken by Danson, geo-referenced data collection in all aspects of their work. Recording and archiving spatially referenced data on dogs, humans and parasite hosts improves the accuracy and efficiency with which such agencies collect relevant data to test the effectiveness of control strategies.

- The range of non-academic agencies influenced by the work may be evidenced directly by the list of partners funded directly in the supporting research grants, which include: Sichuan Centre for Diseases Control and Prevention (China) **[d]**, Ningxia Medical College (China), Xinjiang Medical College (China), Kyrgyz Institute of Livestock, Veterinary Science and Pastures (Kyrgyzstan) and Ministry of Education and Science (Kazakhstan).

The broader impact on disease management of Salford's research is seen most clearly in its influence on national-scale programmes concerned with the control of hydatid (of which AE is one) disease:

- **2010:** Action Plan for Prevention and Control of Echinococcosis in China (2010–2015). The Central People's Government of the People's Republic of China. **[b]** Danson et al's collaborative work in China has impacted directly on the development of an Action Plan to prevent and control hydatid disease. The Action Plan has a five year time frame (2010-2015) and aims to "…*comprehensively promote hydatid disease prevention and control work, to further control the prevalence of hydatid disease, protect people's health, promote economic development and social harmony and stability….".*

  Amongst the objectives of the Action Plan are several that were driven directly by the Salford research including: "…… (*identifying*) ownerless dogs in endemic areas to explore management… international cooperation and exchanges…and the introduction of foreign advanced technology". The ministries tasked with implementing the Action Plan include: Ministry of Health, Ministry of Education, the National Development and Reform Commission, Science and Technology State Ethnic Affairs Commission, Ministry of Public Security, Ministry of Civil Affairs Ministry of Finance, Ministry of Water Resources, Ministry of Agriculture, Ministry of Commerce, State Administration of Radio, State Forestry Administration, and China Women's Federation.

- **2011:** The World Health Organisation, Collaborating Center for Prevention and Treatment of Human Echinococcosis **[c]** recently provided an overview of research on disease distribution and provides clear evidence of the impact of Danson et al's international collaborative work in China, and the link to **[b]**: *"This academic initiative, which now focuses on more specific research issues, has been followed by a national program for surveillance and management of the disease in China (Action Plan, 2010), which involves 14 ministries and is certainly the most ambitious state-funded project ever implemented to diagnose and treat AE in the world."*

- Alveolar Echinococcosis is an important emerging human parasitic disease that is estimated to cost 650,000 disability adjusted life years annually. **[a]** Increased awareness of the extent and impact of the disease, driven in large part by the work of the Salford group and its collaborators, is influencing major initiatives to prevent and control human infection. In addition to the China Action Plan 2010 the World Bank has recently committed $10 million for the control of hydatid and other diseases in Kyrgyzstan where recent research has suggested that changes in land use and animal husbandry, and the removal of veterinary services following the collapse of the communism in the early 1990s, is leading to an emerging new focus of the disease. Knowledge of the spatial characteristics of disease epidemiology, established by Danson, is critical to the success of these initiatives and this knowledge will continue to inform and underpin the fight against this incurable human disease for the next decade and beyond.

5. Sources to corroborate the impact

a) Report of the WHO Informal Working Group on cystic and alveolar echinococcosis surveillance, prevention and control, with the participation of the Food and Agriculture Organization of the United Nations and the World Organisation for Animal Health 22–23 June 2011, Department of Control of Neglected Tropical Diseases WHO, Geneva, Switzerland.
b) Action Plan for Prevention and Control of Echinococcosis in China (2010–2015). The Central People's Government of the People's Republic of China at http://www.gov.cn/zwgk/2010-12/14/content_1765485.htm). In Chinese – translation available from University of Salford
c) Vuitton, D.A., Wang, Q., Zhou, H., Raoul, F., Knapp, J., Bresson-Hadni, S., Wen, H., and Giraudoux, P., 2011, A historical view of alveolar echinococcosis, 160 years after the discovery of the first case in humans: part 1. What have we learnt on the distribution of the disease and on its parasitic agent? Chinese Medical Journal, 124(18), 2943-2953.
d) Letter: Director Sichuan Center for Diseases Control and Prevention.