Institution: University of Salford

Unit of Assessment: UoA A5 Biological Sciences

Title of case study: Transmission and control of parasitic zoonoses

1. Summary of the impact

Transmission and control of parasitic zoonoses focuses on diagnostics development and epidemiological studies on zoonoses, developing approaches for the surveillance, prevention and control of non-vector borne zoonotic pathogens and demonstrating the following impact:

- Making a contribution to the understanding of the transmission and epidemiology of zoonoses, especially echinococcosis, but also toxoplasmosis and African trypanosomiasis;
- Altering traditional views on routes of transmission and control options/surveillance at farm or rural community level using molecular ecology and molecular diagnostic approaches;
- Improving public health and quality of life of the communities and the economies of regions affected through changing national and international public health policy for the surveillance, prevention and control of zoonotic parasitic diseases.

2. Underpinning research

The key researchers and positions they held at the institution at the time of the research are as follows: Professor P Craig (from 1992), Professor MT Rogan (from 1993), Professor Mark Danson (submitted to UoA C17) (from 1994), Professor G Hide (from 1998), Professor Judith Smith (Head of School, from 2010), School of Environment and Life Sciences. Parasitic zoonoses affect both human and animal populations and often exhibit complex life-cycle patterns, thus the transmission ecology becomes important for understanding epidemiology and in consideration of control interventions. The *Cestode Zoonoses Research Group*, which is based in the Biomedical Research Centre, but includes members from several collaborating institutes and acts as an Echinococcus reference centre for DEFRA (UK) and the World Animal Health Organisation (OIE). Research projects include:

- Development and application of sensitive and specific laboratory diagnostic tests for tapeworm and tapeworm cyst infections (echinococcosis, cysticercosis) in humans or animals;
- Study of the unique transmission ecology of *Echinococcus multilocularis* in western China;
- Investigation of the epidemiology of human taeniasis and cysticercosis (caused by *Taenia solium*) in Latin America and Southeast Asia;
- The transmission and control of cystic echinococcosis (*E. granulosus*) in North Africa, East Africa, China and Wales;
- Post-treatment follow-up of human echinococcosis patients using serological tests and a study of the pathology and natural history of hydatid disease in humans.

- **1993 onwards:** Effective diagnostic, detection or surveillance mechanisms for parasitic zoonoses are paramount, Craig developed novel tests (using ELISA, PCR for tissue and faeces) for echinococcosis in canids from the early 1990s [**1**], and Hide for trypanosomiasis in livestock [**2**]. Molecular markers for species or strain specific detection of these pathogens has led to greater understanding of transmission patterns in toxoplasmosis in the UK [**3**] and molecular epidemiology of echinococcosis in western China [4].
- **2000-2008, 2011 onwards:** Cestode zoonoses research in China was supported by the USA Ecology of Infectious Diseases program of NIH/NSF and subsequently by the Wellcome Trust. Field based and community eco-epidemiological research on the zoonosis due to *E. multilocularis* (cause of human alveolar echinococcosis) conducted by Craig in western China (provinces of Gansu, Ningxia, Sichuan) was the first comprehensive assessment in human, canid (dog, fox) and small mammal (rodents, lagomorphs) populations [**4**].
- The application of remote sensing related risk factors to landscape ecology (collaboration-

Prof FM Danson, Geography, Salford) and rodent ecology (collaboration- Prof P Giraudoux, Universite de Franche Comte) to characterise/quantify wildlife habitats and at-risk communities were deforestation and over-grazing were drivers of disease emergence, identifying highly endemic foci on the Tibetan Plateau and showing that landscape ecology, together with low small mammal host biodiversity, correlated with human disease hotspots [**5**].

- The development of molecular tools for the detection and tracking of trypanosome, *Toxoplasma* and microsporidial infections in humans and animals using ITS genes, surface antigen genes, genome sequencing and Mobile Genetic Elements as markers (Hide/Smith). These tools have been applied to specific epidemiological systems such as demonstrating the importance of transmission of *Toxoplasma* in small mammals [**6**] and the role of cattle in sleeping sickness epidemics [**2**].

3. References to the research

Key outputs:

1. Jenkins DJ, Fraser A, Bradshaw H & Craig PS. (2000). Detection of *Echinococcus granulosus* coproantigens in Australian canids with natural or experimental infections. *Journal of Parasitology*, 86: 140-145. DOI
2. Cox, A., Tosas, O., Tilley, A., Picozzi, K., Coleman, P.G., Hide, G., and Welburn, S.C. (2010). Constraints to estimating the prevalence of trypanosome infections in East African Zebu Cattle. *Parasites and Vectors*, 3: 82-90. DOI **(REF 2)**
3. Morley, E.K., Williams, R.H., Hughes, J.M., Thomasson, D., Terry, R.S., Duncanson, P., Smith, J.E. and Hide, G. (2008). Evidence that primary infection of charollais sheep with *Toxoplasma gondii* may not prevent foetal infection and abortion in subsequent lambings. *Parasitology*: 135, 169-173. DOI **(REF 2)**
4. Craig PS, Giraudoux P, Shi D, Bartholomot B, Barnish G, Delattre P, Quere JP, Harraga S, Bao G, Wang Y, Lu F, Ito A, & Vuitton DA. (2000). An epidemiological and ecological study of human alveolar echinococcosis transmission in south Gansu, China. *Acta Tropica*, 77: 167-177. DOI
5. Giraudoux P, Raoul F, Pleydell, D, Li, T, Han, X, Qiu, J, Xie, Y, Wang, H, Ito, A & Craig, P S. (2013). Drivers of *Echinococcus multilocularis* transmission in China: host biodiversity, landscape or climate? *PLoS Neglected Tropical Diseases*, 7, p.e2045. DOI **(REF 2)**
6. Thomasson D, Wright E, Hughes J, Dodd N, Cox A, Boyce K, Gerwash O, Abushahama M, Lun Z, Murphy G, Rogan MT, Hide G. (2011). Prevalence and co-infection of *Toxoplasma gondii* and *Neospora caninum* in *Apodemus sylvaticus* in an area relatively free of cats. *Parasitology*, 138: 1117-1123. DOI **(REF 2)**

Key Grants:

7. **2011:** Multi-species transmission of Echinococcus on the Tibetan plateau, Wellcome Trust, £462,630.00. Principal Investigator: P Craig (80%), co PI- M Rogan (20%).
8. **2005:** Ecosystem disturbance and multiscale transmission of zoonotic wildlife pathogen United States - National Institutes of Health/National Science Foundation, £349,160.00. Investigators: PI- P Craig (60%), co PI M Danson (40%).
9. **2002:** New insights in the epidemiology and control of *Taenia solium* taenosis/ cysticercosis. Burroughs Wellcome Initiative (USA-UK), £302,835, PI: P Craig
10. **2000:** Parasitic zoonosis (echinococcosis) transmission in China US NIH, £465,532.00.Investigators: PI- P Craig (75%), M Danson (25%).
11. **1998**: Cystic echinococcosis (hydatidosis) in the Eastern Mediterranean and Middle East - Diagnostic tools for public health and epidemiology. European Commision 450,000 euros, PI: P Craig

4. Details of the impact

Context: Diagnostics development and epidemiological studies on echinococcosis from 2000 have influenced national and international public health policy for surveillance, prevention and control of that zoonosis, and the inclusion (2006) of echinococcosis in the World Health Organization (WHO) priority list of Neglected Zoonotic Diseases. The annual cost of treating cases and economic losses to the livestock industry probably amounts to US$ 2 billion. Research on molecular ecology of the zoonoses toxoplasmosis and African trypanosomiasis has altered traditional views on routes of transmission and control options at farm or rural community level [**a**].

- Application of the *Echinococcus* copro ELISA test developed by Craig to screen farm dogs in mid Wales showed increased levels of transmission over a >10 year period [**b**] and resulted in the subsequent initiation in 2008 by the Welsh Assembly Government of a dog-focused pilot echinococcosis control programme in the endemic region [**c**]. This surveillance tool has been recommended for use by WHO since 2001 [**d**] and already copied and applied to epidemiological studies and *Echinococcus* control programmes in Argentina, Chile, Australia and China [**e**].
- Our collaborative based research in western China provided community data and surveillance approaches that under-pinned the decision of the Ministry of Health China to undertake (from 2006/7) the world`s largest echinococcosis control programme. This National Echinococcosis control programme continues to run in China through the *2010-2020 Action Plan* with US$100 million allocation wherein coproantigen tests for canine echinococcosis, based on our research, are used as a key surveillance tool across 8 Provinces [**e**].
- In 2010 we formed a Salford-based enterprise laboratory *Cestode Diagnostics* as a testing, development and training unit for cestode parasite detection, diagnosis and molecular typing of animal and human derived samples which has also recently highlighted pathological problems of larval cestodes in mammals in zoos or safari parks in UK [**g**]. An *Echinococcus* OIE/ DEFRA licensed reference laboratory under Craig has operated in Salford since 1999.
- Inter-disciplinary collaboration between parasitologist (Craig, Salford), mammalian ecologist (Giraudoux, Franche-Comte) and geographer (Danson, Salford), to study the transmission of alveolar echinococcosis in China has resulted in wider implications and impact for role of landscape ecology in the emergence of non-vector borne zoonotic pathogens associated with small mammal populations [**h**].
- Our collaborative work on the development of molecular tools for understanding human and animal trypanosomiasis in Africa (Hide, Salford; S.Welburn, Edinburgh) has demonstrated the importance of cattle as a reservoir for human sleeping sickness [**i**] and this has led to the development of the "Stamp out Sleeping Sickness (SOS)" programme in Uganda and contributed to the "Research in Use" scheme **[j].**
- **2011:** The World Health Organisation, Collaborating Center for Prevention and Treatment of Human Echinococcosis recently provided an overview of research on disease distribution [**k**] and refers to the impact of Craig et al's international collaborative work in China: *"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."*

5. Sources to corroborate the impact

a) *The Control of Neglected Zoonotic Diseases: Community-based interventions for prevention and control*. Report 2011, WHO (Geneva); www.who.int/neglected_diseases/zoonoses/en/

b) Buishi I, Walters T, Guildea Z, Craig PS & Palmer S. (2005). Reemergence of canine *Echinococcus granulosus* infection, Wales. *Emerging Infectious Diseases*, 11, 568-571.

c) www.defra.gov.uk/animal-diseases/zoonotic/; Zoonoses Report UK 2011 (December 2012), Echinococcosis pp 42-44.

d) *WHO/OIE Manual on Echinococcosis in Humans and Animals: a Public Health Problem of Global Concern*. (2001). Eds J Eckert, MA Gemmell, FX Meslin, ZS Pawlowski. World Organisation for Animal Health, Paris

e) *Action Plan for Prevention and Control of Echinococcosis in China (2010-2015)*. The Central People`s Government of the People's Republic of China (http://www.gov.cn/zwgk/2010-12/14/ciontent_1765485.htm; in Chinese translation available);

f) Testimonial from Director, Sichuan Center for Diseases Control and Prevention

g) Boufana B, Stidworthy MF, Bell S et al.Craig PS. (2012). *Echinococcus* and *Taenia* spp. from captive mammals in the United Kingdom. *Veterinary Parasitology*, 190,95-103.Cestode Diagnostics impact (http://www.star.salford.ac.uk/page/Cestode_Diagnostics)

h) Vuitton DA *et al* (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, 2943-2953.(Contribution of Craig reported)

i) *World Health Organization* web site paper by Hide included. http://www.who.int/trypanosomiasis_african/country/en/

j) DFID Animal Health Programme "Research into Use". Reported in http://r4d.dfid.gov.uk/PDF/Outputs/ResearchIntoUse/AHP01.pdf

k) 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. http://whqlibdoc.who.int/publications/2011/9789241502924_eng.pdf