Viruses and cancer, cats and cattle: A tribute to Bill Jarrett

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Professor William (Bill) Fleming Hoggan Jarrett, veterinary pathologist, was born in Glasgow, Scotland, UK, on 2 January 1928 and died on 27 August 2011. He is recognised for major contributions in the fields of virology, oncology and parasitology, including the discovery of feline leukaemia virus (FeLV), the development of a vaccine against lungworm (*Dictyocaulus viviparus*) infestation in cattle and identifying the synergistic role of bovine papillomaviruses (BPVs) and bracken fern (*Pteridium* spp.) in inducing neoplasia of the alimentary and urinary tracts in cattle. These important discoveries were made during a long career based in Glasgow, interrupted by brief sojourns in Kenya to work on *Theileria parva*, the cause of East Coast fever in cattle, and in the USA to work on retroviruses with Robert Gallo. Bill graduated from the Glasgow Veterinary College with a veterinary degree in 1949, undertook a PhD in pathology and was Professor of Veterinary Pathology at the University of Glasgow from 1968 until he retired in 1990.

One of Bill Jarrett’s most important contributions to science was the discovery of FeLV, a simple retrovirus causing leukaemia and other haematopoietic neoplasms in cats. Bill was intrigued by the high frequency of lymphosarcoma (lymphoma) observed in cats in the West of Scotland by Harry Pfaff, a Glasgow veterinary practitioner. Retroviruses were known to induce haematopoietic neoplasms in chickens (Rous, 1910) and mice (Furth and Strumia, 1931; Friend, 1957; Gross, 1957). Shope fibroma virus had been identified as the cause of mesenchymal tumours in the Eastern cottontail rabbit (*Sylvilagus floridanus*) (Shope, 1932). However, a role for viruses as aetiological agents in neoplasms in other mammalian species was yet to be established. Bill isolated FeLV in cell culture from cats with lymphosarcoma and published his findings in *Nature* in 1964 (Jarrett et al., 1964a,b). This seminal discovery stimulated interest in oncogenic viruses throughout the world and paved the way for the discovery of human T cell leukaemia virus type I, the cause of adult T cell leukaemia/lymphoma in humans (Poiesz et al., 1980; Miyoshi et al., 1981; Gallo et al., 1983), and the subsequent discovery of human immunodeficiency virus type 1 (Barré-Sinoussi et al., 1983; Gallo et al., 1984; Popovic et al., 1984).

In a review article published in this issue of *The Veterinary Journal*, Professors Brian Willett and Margaret Hosie, both at the University of Glasgow, highlight recent advances that have been made in understanding the pathogenesis and control of FeLV (Willett and Hosie, 2013). Early studies elucidated the biological properties of FeLV in vitro and in vivo, in particular defining the transmissibility of the virus among cats (Jarrett et al., 1973). This was followed by studies on the immunology of FeLV, unravelling the complexities of viral latency in the host and identifying viral integration sites associated with neoplasia (Neil et al., 1984).
Effective diagnostic tests and vaccines against FeLV have been developed and rapid immunochromatographic assays are now available for detection of FeLV in clinical veterinary practice. More recently, new insights into the molecular and cellular biology of FeLV have refined our understanding of the virus. The cellular receptors used by FeLV subtypes for entry into cells have been identified, including the thiamine transporter THTR1 (the receptor for FeLV-A), the phosphate symporters Pit-1 and Pit-2 (the receptors for FeLV-B) and the haem transporter FLVCR1 (the receptor for FeLV-C) (Willett and Hosie, 2013). Such studies have contributed to an increased understanding of several immune deficiency syndromes and anaemias in humans, illustrating the value of comparative pathology, a theme close to Bill Jarrett’s heart.

In his early career, Bill Jarrett worked with the team at the University of Glasgow that developed the first effective vaccine against a nematode parasite. Oral administration of live irradiated third stage larvae of the lungworm *Dictyocaulus viviparus*, a nematode parasite. Oral administration of live irradiated third stage larvae of the lungworm *D. viviparus* induced protective immunity in cattle against this important respiratory pathogen (Jarrett et al., 1958, 1960). The vaccine has been in continuous production since it was introduced in 1965 and remains the only effective vaccine against a nematode parasite available commercially.

The acute eye of the discerning pathologist sees patterns in the daily routine of diagnostic work. This was the case when Bill Jarrett recognised a close geographical match between the distribution of bracken fern and the occurrence of neoplasms of the alimentary and urinary tracts in cattle in the Highlands of Scotland (Jarrett et al., 1978a,b). Bill brought his virology knowledge into this investigation, leading to the identification of BPVs as key initiating factors in the development of these tumours. Immunosuppressants (such as sesquiterpenes) and carcinogens (such as quercetin and ptaquiloside) in bracken fern act in synergy with BPVs to induce a range of epithelial and vascular tumours of the alimentary (BPV type 4) and urinary (BPV types 1 and 2) tracts. Work on vaccination against BPVs by Bill and his colleagues (Jarrett et al., 1990) laid the ground work for the development of a vaccine against subtypes of human papillomaviruses causing cervical cancer in women. Vaccination against human papillomaviruses is now offered routinely to young women in the UK and many other countries for the prevention of cervical cancer (Campo and Roden, 2010).

One of Bill Jarrett’s longstanding interests was in the aetiology of canine hepatitis. In a series of experiments in dogs, Bill found evidence of a transmissible agent causing acute and chronic hepatitis and cirrhosis; he suggested that this agent should be called canine acidophil cell hepatitis virus (Jarrett and O’Neil, 1985; Jarrett et al., 1987). The presence of this virus has not been verified subsequently, but it is intriguing that a hepatitis C-like virus has been frequently, but it is intriguing that a hepatitis C-like virus has been identified in dogs recently (Kapoor et al., 2011; Burbelo et al., 2012). The active scientific mind never rests in its quest for new answers to old questions.

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