445  Ferret transmission model for tuberculosis. T. Gupta, S. Helms, K. Sakamoto, S. Harvey, T. Ross, C. Whalen, R. Karls, and F. Quinn*, University of Georgia, Athens, GA.

Tuberculosis (TB) is a persistent infectious disease that threatens the health of people and numerous mammalian animal species worldwide. Estimates are that 9 million new human TB cases occur annually while animal illness rates are higher but the actual numbers are unknown. Epidemiology studies indicate that transmission among close contacts is the driving force behind TB epidemics. Until successfully treated or until infected animals are removed, cases will continue to transmit bacilli to contacts. Since antibiotic treatment for most infected animals is not practical, and a vaccine that generates sterilizing immunity has not been developed, a vaccine that controls disease transmission may be the current best path forward. Unlike rodents, infected larger animals including cattle and non-human primates (NHPs) can effectively transmit the bacilli to naive hosts via the aerosol route; however, routine work with statistically significant numbers of cattle and NHPs is cost-prohibitive. Thus, an appropriate small animal TB transmission model for assessing vaccines is needed. Ferrets are widely employed to study the transmissibility of influenza viruses and other respiratory agents, but thus far, no studies examining these parameters for Mycobacterium bovis (Mb) and M. tuberculosis (Mt) have been reported. We know that mice and guinea pigs intratracheally or intravenously infected with virulent Mb and Mt bacilli develop acute disease and ultimately succumb. This is not the disease process observed in humans and animals in natural settings. In high-exposure locations, TB contacts have been found to develop acute disease but remain TST-negative and free of the pathogen, remain TST-negative but carry viable bacilli in their airways, or become TST-positive but remain culture negative. In other words, natural transmission results in variable disease responses. Our team has generated exciting preliminary data demonstrating that ferrets can become infected when given intratracheal Mt bacilli, but most importantly, transmission occurs when infected transmitter animals interact with naïve sentinels co-housed over the course of at least 2 mo. Additionally, the TB disease states described above are also observed in naturally-infected ferrets.

Key Words: tuberculosis, transmission model

446  The current status of bovine tuberculosis in the world. A. Perera*, USDA APHIS VS/IS Mexico, Mexico City, Mexico.

Tuberculosis is an important disease in animals and humans causing substantial morbidity, mortality, and economic loss. Significant variation exists in ways organisms of the M. tuberculosis complex affect animals and humans; however, there are also important intersections between animals and humans. The best example is the occurrence of M. bovis disease in humans and animals. The genus Mycobacterium includes several species that cause TB in humans and other animals. The M. tuberculosis complex includes M. tuberculosis, M. cannetti, M. africanum, M. bovis, M. pinnipedii, M. mungi, M. caprae, and M. microti. The tubercle bacillus infects an estimated 2 billion people with 95% of the cases in developing countries. TB is a leading cause of infectious disease-related death worldwide, estimated to cause 1.5 to 2 million yearly. Zoonotic tuberculosis (TB) in people is caused by Mycobacterium bovis, which belongs to the M. tuberculosis complex. Cattle are the most important animal reservoir for exposure of humans, but the disease affects other species and can become established in wildlife. It often affects sites other than the lungs, such as lymph nodes. In many cases, it is clinically indistinguishable from TB caused by M. tuberculosis. In 2015, there were an estimated 149,000 new human cases of zoonotic TB globally, and 13,400 deaths due to zoonotic TB. Africa carries the heaviest burden of disease and death, followed by Southeast Asia. The true burden is likely underestimated due to a lack of routine surveillance data. Risk factors: The most common route of transmission to humans is through food. Airborne infections and direct contact with infected animals pose a risk to people with frequent direct contact with infected animals or contaminated animal products. Common laboratory diagnostic procedures do not differentiate M. tuberculosis from M. bovis leading to under-diagnosis of zoonotic TB. Zoonotic TB poses special challenges for patient treatment and recovery. M. bovis is naturally resistant to pyrazinamide, one of 4 medications used in standard first-line anti-TB treatment regimen. Most TB patients begin treatment without drug susceptibility testing, so patients with zoonotic TB may receive inadequate treatment. Zoonotic TB in humans is often extra-pulmonary and may be misdiagnosed, and therefore initiation of treatment delayed.

Key Words: tuberculosis, diagnostic procedures

447  Development of a subunit vaccine for bovine tuberculosis. N. Guy1, N. Rawlyk1, M. Bains2, O. Iheioha1, Z. Lim1, K. Bock1, S. Walker1, C. Wheler1, V. Gerds1, J. Chen1, R. E. Hancock2, and A. A. Potter1, 1Vaccine and Infectious Disease Organization-InterVac, Saskatoon, SK, Canada, 2Centre for Microbial Disease and Immunity Research, Vancouver, BC, Canada.

Bovine tuberculosis remains a major threat to the dairy industry in North America. Although the disease has nearly been eliminated in the United States and Canada, sporadic outbreaks occur with significant economic consequences to the industry. For example, >45,000 cattle were quarantined and >12,000 animals were destroyed in a recent outbreak in Western Canada that could be traced back to 6 cows that initially tested positive for bovine tuberculosis. Wildlife reservoirs, including bison and elk, that are known to transmit the disease to cattle, significantly hamper effective disease control and our ability to internationally trade live animals and meat products. Vaccines are urgently needed that not only prevent the disease in animals but also distinguish infected from vaccinated animals (DIVA vaccine). We are currently using reverse vaccinology methodology to develop a novel subunit vaccine and companion diagnostics that will meet these requirements. Reverse vaccinology is a relatively new approach to vaccine development. It is based on an unbiased screening of large numbers of potential vaccine candidates (proteins) in animal models. We have produced >80 different proteins that are currently being evaluated for their ability to protect calves from bovine tuberculosis. Promising vaccine candidates will be further characterized and optimized by formulation with adjuvants. The talk will provide an update on the status of the project.

Key Words: bovine tuberculosis, vaccine
Bovine tuberculosis (bTB) is a chronic disease that limits livestock productivity and represents a significant threat to human health with annual economic losses estimated at over $3 billion. While the disease is well controlled in the developed world, it remains endemic in many developing countries. Given the importance of the dairy and livestock industry to inclusive agricultural transformation, improved nutrition, and overall economic development, there is an increased emphasis on improving animal productivity and intensive farming techniques. However, in the absence of an effective bTB control program, intensification of dairy production is expected to drive an increase in bTB prevalence and associated animal and human disease and reduction in animal productivity (~10% reduction each in milk productivity and reproductive efficiency, and 20% loss in weight of bTB infected animals). While the implementation of bTB control programs has been documented to result in reduction in human death and suffering together with an almost 10-fold return on investment in animal productivity and economic benefit to farmers, the upfront costs associated with implementing the test and cull program in developing countries where the majority of livestock are owned by small and marginal farmers is not feasible for social and economic reasons. Hence, there is an increasing recognition of the urgent need to accelerate the development and implementation of rational evidence-based approaches to control bTB. This presentation will describe a recently initiated program in India and Ethiopia to assess vaccines to block onward transmission (cattle-to-cattle or cattle-to-other livestock, human or wildlife), as well as develop and validate fit-for-purpose diagnostic assays to differentiate vaccinated from infected animals, together providing a strong foundation for the development of effective bTB control programs in developing countries.

**Key Words:** bovine tuberculosis, vaccine