2013-03-22 007 Paratuberculosis databases updated (2013-03-20)

New publications in the PARATUBERCULOSIS database (1348-1358)

1348 Speybroeck, N., Williams, C.J., Lafia, K.B., Devleesschauwer, B., Berkvens, D. (2012)
Estimating the prevalence of infections in vector populations using pools of samples
Medical and Veterinary Entomology, 26, 361-371

Several statistical methods have been proposed for estimating the infection prevalence based on pooled samples, but these methods generally presume the application of perfect diagnostic tests, which in practice do not exist. To optimize prevalence estimation based on pooled samples, currently available and new statistical models were described and compared. Three groups were tested: (a) Frequentist models, (b) Monte Carlo Markov-Chain (MCMC) Bayesian models, and (c) Exact Bayesian Computation (EBC) models. Simulated data allowed the comparison of the models, including testing the performance under complex situations such as imperfect tests with a sensitivity varying according to the pool weight. In addition, all models were applied to data derived from the literature, to demonstrate the influence of the model on real-prevalence estimates. All models were implemented in the freely available R and OpenBUGS software and are presented in Appendix S1. Bayesian models can flexibl y take into account the imperfect sensitivity and specificity of the diagnostic test (as well as the influence of pool-related or external variables) and are therefore the method of choice for calculating population prevalence based on pooled samples. However, when using such complex models, very precise information on test characteristics is needed, which may in general not be available

1349 Santema, W.J., Poot, J., Segers, R.P.A.M., Van den Hoff, D.J.P., Rutten, V.P.M.G., Koets, A.P. (2012)
Early infection dynamics after experimental challenge with Mycobacterium avium subspecies paratuberculosis in calves reveal limited calf-to-calf transmission and no impact of Hsp70 vaccination
Vaccine, 30, 7032-7039

Efficient control of bovine paratuberculosis is hampered by lack of a vaccine. The purpose of this study was to evaluate efficacy of a candidate vaccine, consisting of recombinant Mycobacterium avium subspecies paratuberculosis (MAP) Hsp70 with DDA adjuvant, in calves experimentally infected with MAP. Four groups of 14 animals each were used. Animals in group 1 and 2 were all vaccinated with Hsp70/DDA at day 0, 84, 168 and 357, and those in group 3 and 4 were non-vaccinated controls. In each group half (n = 7) of the animals were challenged and the remaining half served as contacts. Blood and fecal samples were collected at three week intervals until day 588, and subsequently all animals were subjected to necropsy. The primary outcomes assessed were fecal culture (FC) of MAP, tissue colonization of MAP, and transmission of infection to contact animals. The kinetics of MAP shedding in feces of challenged animals showed a peak around 130 days post-challenge, irrespective of v accination status. At necropsy no differences in the level of tissue colonization between vaccinated animals and controls were observed in the challenged groups. Only one contact animal (non-vaccinated) was positive at necropsy, indicating limited to no transmission within groups. These findings indicate that Hsp70/DDA vaccination does not influence early infection dynamics after experimental infection. However, early shedding of MAP in calves did not result in efficient transmission of infection to contact animals. The latter implies that introduction of an infected calf in a cohort of susceptibles has limited consequences for spread of infection.

1350 Click, R.E. (2012)
Alteration of GI symptoms in a cow with Johne disease by the dietary organosulfur, 2-mercaptoethanol
Virulence, 3, 543-545

Sub-phenotypes of inflammatory bowel disease (IBD)-Crohn disease, ulcerative colitis and some cases of irritable bowel syndrome-are generally considered a consequence of gastrointestinal inflammation of unknown etiology. Conventional therapy and more recently biologic agents, all with varying degrees of drawbacks, have resulted in improved control of these diseases. However, as the incidence and prevalence continue to rise, needs for prevention, permanent remission and cures remain unmet, plus there still remain needs for improved control of symptoms, such as pain and diarrhea. The case report herein describes a serendipitous, novel means for curtailing these symptoms associated with a bovine gastrointestinal disease that may have applicability for patients with diseases characterized by abdominal-visceral pain and diarrhea

1351 Pierce, E.S. (2012)
Free-ranging Rocky Mountain bighorn sheep and an outbreak of inflammatory bowel disease along the Clark Fork River in Plains, Montana
Virulence, 3, 546-550

Nine individuals with ulcerative colitis or Crohn disease grew up or lived in Plains, Montana, a 1,200-person community adjacent to the Clark Fork River near herds of free ranging Rocky Mountain bighorn sheep. This inflammatory bowel disease outbreak is similar to others that have occurred along rivers contaminated by animal feces

1352 Mundo, S.L., Gilardoni, L.R., Hoffman, F.J., Lopez, O.J. (2013)
Rapid and Sensitive Method To Identify Mycobacterium avium subsp paratuberculosis in Cow's Milk by DNA Methylase Genotyping
Applied and Environmental Microbiology, 79, 1612-1618

Paratuberculosis is an infectious, chronic, and incurable disease that affects ruminants, caused by Mycobacterium avium subsp. paratuberculosis. This bacterium is shed primarily through feces of infected cows but can be also excreted in colostrum and milk and might survive pasteurization. Since an association of genomic sequences of M. avium subsp. paratuberculosis in patients with Crohn's disease has been described; it is of interest to rapidly detect M. avium subsp. paratuberculosis in milk for human consumption. IS900 insertion is used as a target for PCR amplification to identify the presence of M. avium subsp. paratuberculosis in biological samples. Two target sequences were selected: IS1 (155 bp) and IS2 (94 bp). These fragments have a 100% identity among all M. avium subsp. paratuberculosis strains sequenced. M. avium subsp. paratuberculosis was specifically concentrated from milk samples by immunomagnetic separation prior to performing PCR. The amplicons were ch aracterized using DNA methylase Genotyping, i.e., the amplicons were methylated with 6-methyl-adenine and digested with restriction enzymes to confirm their identity. The methylated amplicons from 100 CFU of M. avium subsp. paratuberculosis can be visualized in a Western blot format using an anti-6-methyl-adenine monoclonal antibody. The use of DNA methyltransferase genotyping coupled to a scintillation proximity assay allows for the detection of up to 10 CFU of M. avium subsp. paratuberculosis per ml of milk. This test is rapid and sensitive and allows for automation and thus multiple samples can be tested at the same time

1353 More, S.J., Sergeant, E.S.G., Strain, S., Cashman, W., Kenny, K., Graham, D. (2013)
The effect of alternative testing strategies and bio-exclusion practices on Johne's disease risk in test-negative herds
Journal of Dairy Science, 96, 1581-1590

Herd classification is a key component of national Johne's disease (JD) control programs. Herds are categorized on the basis of test results, and separate sub-programs are followed for test-positive and test-negative herds. However, a test-negative herd result does not necessarily equate to JD freedom for reasons relating to disease pathogenesis and available diagnostic tests. Thus, in several countries, JD control programs define test-negative herds as having a "low risk" of infection below a specified prevalence. However, the approach is qualitative, and little quantitative work is available on herd-level estimates of probability of

freedom in test-negative herds. This paper examines the effect over time of alternative testing strategies and bio-exclusion practices on JD risk in test-negative herds. A simulation model was developed in the programming language R. Key model inputs included sensitivity and specificity estimates for 3 individual animal diagnosti c tests (serum ELISA, milk ELISA, and fecal culture), design prevalence, testing options, and testing costs. Key model outputs included the probability that infection will be detected if present at the design prevalence or greater (herd sensitivity; Sell), the probability that infection in the herd is either absent or at very low prevalence (i.e., less than the design prevalence; ProbF), the probability of an uninfected herd producing a false-positive result [P(False+)], and mean testing cost (HerdCost) for different testing strategies. The output ProbF can be updated periodically, incorporating data from additional herd testing and information on cattle purchases, and could form the basis for an output-based approach to herd classification. A high ProbF is very difficult to achieve, reflecting the low sensitivity of the evaluated tests. Moreover, ProbF is greatly affected by any risk of introduction of infection, decreasing in herds with poor bio-exclusion practices despite ongoing negative test results. The value of P(False+) was substantial when tests with imperfect specificity were used. Testing strategies can substantially influence testing costs but with little effect on test performance. This study illustrates an output-based approach to herd classification, with potential for national and field applications

1354 Billinis, C. (2013)
Wildlife diseases that pose a risk to small ruminants and their farmers
Small Ruminant Research, 110, 67-70

Infectious pathogens from wild animals have become increasingly important throughout the world in recent years, as they have had a substantial impact in livestock and human health. A large number of pathogens (61% of the 1415 currently identified human pathogens within 313 different genera) are zoonotic and can infect multiple animal species. Multi-host pathogens are predominant among animal and human emerging diseases. Multi-host pathogens (including all zoonotic agents, pathogens that can infect more than one taxonomic order and pathogens that can infect wildlife hosts) have a higher relative risk for emergence than species-specific pathogens. Of 800 zoonotic diseases currently identified, 619 (77%) are caused by pathogens that affect wildlife; of 125 emerging zoonotic diseases, 113 (90%) affect wildlife. Of the diseases that have emerged in the last few decades around 75% are of wildlife origin. Many factors influence changes in disease incidence, including economic, cli matic and microbiological effects. Increasingly, close interaction of humans and livestock with wild animals has led to increased frequency of zoonotic infections. Forest clearance and movement of animals or animal products are factors, which pose significant risks of introducing disease into a new region. Changing climate affects disease incidence by changes in land use or animal production practices, as well as by movement or changes in distribution of animal reservoirs or insect vectors. Local increases in biting midges or mosquito numbers, changes in the distribution of known vector species and/or recruitment of novel vector species, have increased the risk of spread or introduction of diseases. Pathogen evolution may occur in response to changes of which humans are not aware. The evolution may be occurring in many hosts, currently poorly monitored. Microbial evolution may affect the extent to which established methods of diagnosis can detect infectious agents. Other end emic diseases may also change in incidence for largely unknown reasons. Increased information on prevalence in a wide range of hosts will increase our understanding of these reasons. Wildlife can play an important role in the epidemiology of small ruminant and human diseases, by representing a source of disease via various transmission routes. Recent studies in infections of wildlife in Europe have highlighted the impact on small ruminant health. In Greece, blood/organ samples were collected from 60 wild deer and 140 wild boars (2006-2011). Serum samples were tested for presence of antibodies against Toxoplasma gondii,Neospora caninum, Mycobacterium avium subsp. paratuberculosis, Chlamydophila, Salmonella and Trichinella spirallis, by using appropriate immunodiagnostic techniques. Tissue samples were examined for Mycobacterium bovis by using PCR. In serum samples from deer, antibodies against T. gondii, N. caninum and Chlamydophila were detected in 15%, 5% and 5% of samples, respectively. In serum samples from wild boars, antibodies against Salmonella, T. gondii and T. spirallis were

detected in 15%, 5% and 5% of samples, respectively. No M. bovis was found in tissue samples. In Spain, Bluetongue virus, Brucella spp., Coxiella bumetii and M. avium were detected in many wild cervid species. Spanish wild boars have been found to be greatly exposed to Salmonella spp., an important small ruminant intestinal pathogen. In Austria, Spain and Poland, Anaplasma phagocytophilum has been detected in various cervids. Finally, in Poland and Spain, wild deer and wild boars were found to be exposed to T. gondii and N. caninum. The results indicate that wildlife may be carriers of several pathogens, which can be transmitted to domestic small ruminants and their farmers. It is noteworthy that samples from many European countries will be collected and tested to ensure a broader evaluation of the epidemiological role of wildlife.

1355 Windsor, P.A. (2013)
Understanding the efficacy of vaccination in controlling ovine paratuberculosis
Small Ruminant Research, 110, 161-164

It is believed that so-called 'S' strains of Mycobacterium avium subsp. paratuberculosis, the causative agent of ovine paratuberculosis, were introduced into Australia in Merino sheep from New Zealand in the 1960s. The disease was first diagnosed in Australia in the central tablelands of New South Wales in the early 1980s, but caused few problems until the mid 1990s, when the current epidemic of the disease emerged to become one of the most important endemic diseases in Australia. Paratuberculosis continues to spread well beyond the original infected region in New South Wales, with prevalence rising in all states of the country, except South Australia and Queensland. A research project on Gudair (TM) vaccine, which led to the licensing of the product in 2002, identified that numbers of vaccinated sheep that died of the disease, or shed the causative agent declined by 90% in the first generation of vaccinated sheep. Vaccination and a risk-based trading scheme known a s the ABC scheme (Assurance Based Credit points accrued for evidence suggestive of disease absence, currently including points for paratuberculosis vaccination) that uses a national sheep vendor declaration for sale of sheep, are now the main tools used for the control of the disease in most Australian states. However, vaccination for paratuberculosis remains controversial in some parts of the world, largely based on concerns relating to the efficacy of the vaccine in decreasing the risk of infection and transmission of the organism. The Australian experience has shown that vaccination against paratuberculosis quickly eliminates the significant mortalities in infected, high prevalence flocks. However, our applied research has shown that shedding of M. avium subsp. paratuberculosis from vaccinated sheep may persist for many years after commencing of vaccination programmes. In a longitudinal study of 11 flocks over 6 years, where 3- and 4-year-old animals were monitored every 2 years, we observed a substantial reduction in the prevalence of microbial shedding of >75% following vaccination, although in four flocks such a reduction was not evident. Further, in a study of 41 flocks where vaccination of lambs had been applied for 6 years, shedding persisted in the majority of flocks (81) and risk factor studies in these flocks indicated a number of management factors may be important in persistence of the disease. Stray sheep, failure to vaccinate wethers, introduction of unvaccinated sheep into the flock and use of commercial 'contractors' to do the vaccinations were associated with increased prevalence of paratuberculosis in vaccinated flocks. Improvement of farm biosecurity and correct vaccination schedules of all sheep in a flock are suggested as important management interventions to optimize the protection offered by Gudair (TM). A recent study on Kangaroo Island has confirmed that where a majority of these practices are rigorously ap plied, eradication of the disease is potentially possible. Despite the persistence of shedding in vaccinates in many parts of the country, vaccination to control paratuberculosis in Australia has been of enormous benefit to the sheep industry and rural communities and this needs to be recognized internationally.

1356 Dobson, B., Liggett, S., O'Brien, R., Griffin, J.F.T. (2013)
Innate immune markers that distinguish red deer (Cervus elaphus) selected for resistant or susceptible genotypes for Johne's disease
Veterinary Research, 44, Article Number: 5 DOI: 10.1186/1297-9716-44-5 Published: JAN 24 2013-While many factors contribute to resistance and susceptibility to infectious disease, a

major component is the genotype of the host and the way in which it is expressed. Johne's disease is a chronic inflammatory bowel disease affecting ruminants and is caused by infection with Mycobacterium avium subspecies paratuberculosis (MAP). We have previously identified red deer breeds (Cervus elaphus) that are resistant; have a low rate of MAP infection and do not progress to develop Johne's disease. In contrast, susceptible breeds have a high rate of MAP infection as seen by seroconversion and progress to develop clinical Johne's disease. The aim of this study was to determine if immunological differences exist between animals of resistant or susceptible breeds. Macrophage cultures were derived from the monocytes of deer genotypically defined as resistan t or susceptible to the development of Johne's disease. Following in vitro infection of the cells with MAP, the expression of candidate genes was assessed by quantitative PCR as well as infection rate and cell death rate. The results indicate that macrophages from susceptible animals show a significantly higher upregulation of inflammatory genes (iNOS, IL-1 alpha, TNF-alpha and IL-23p19) than the macrophages from resistant animals. Cells from resistant animals had a higher rate of apoptosis at 24 hours post infection (hpi) compared to macrophages from susceptible animals. The excessive expression of inflammatory mRNA transcripts in susceptible animals could cause inefficient clearing of the mycobacterial organism and the establishment of disease. Controlled upregulation of inflammatory pathways coupled with programmed cell death in the macrophages of resistant animals may predispose the host to a protective immune response against this mycobacterial pathogen

1357 Hruska, K., Kaevska, M. (2012)
Mycobacteria in water, soil, plants and air: a review
Veterinarni Medicina, 57, 623-679

Amazingly, despite the 24 143 papers on mycobacteria, indexed in the Web of Science database during the last six years, published by 67 008 authors from 13 128 organizations located in 166 countries or territories, internationally accepted legal directives on how to control the public health risk associated with environmental mycobacteria have yet to be developed. Mycobacteria are human and animal pathogens, causing not only tuberculosis and leprosy, but mycobacterioses of skin, soft tissues and lung. Due to their cell wall composition and their adaptability mycobacteria can survive in different habitats for years. Their immunomodulatory ability has been recognised for more than 50 years and hundreds of papers published during the last two decades have demonstrated that small chemical products derived from mycobacterial cells participate in inflammatory pathways involved the pathogenesis of important human diseases like Crohn's disease, asthma, type 1 diabetes mellitus, psoriasis, arthrosis, Blau syndrom, sarcoidosis, autism etc. Mycobacteria can influence inflammatory pathways not only as live organisms, but also by means of components derived from dead cells. Pasteurisation or cooking does not affect this ability. Hence, how many mycobacterial cells are ingested, what factors play a role concurrently, and how long the harmful effect persists become important questions. This paper presents only a short review based on selected papers about mycobacteria in water, soil, plants and air with the aim of attracting attention to this significant global problem and of making the first steps towards protection of people. Selected bibliographic references of published data from 2007 to 2012 are presented in easy-to-navigate tables

1358 Knust, B., Patton, E., Ribeiro-Lima, J., Bohn, J.J., Wells, S.J. (2013)
Evaluation of the effects of a killed whole-cell vaccine against Mycobacterium avium subsp paratuberculogis in 3 herds of dairy cattle with natural exposure to the organism
Javma-Journal of the American Veterinary Medical Association, 242, 663-669

Objective-To evaluate effects of vaccination with a killed whole-cell vaccine against Mycobacterium avium subsp paratuberculosis (MAP) on fecal shedding of the organism, development of clinical paratuberculosis (Johne's disease [JD]), milk production, measures of reproduction, and within-herd longevity of dairy cattle naturally exposed to MAR Design-Controlled clinical trial. Animals-200 vaccinated

and 195 unvaccinated (control) dairy cows from 3 herds in Wisconsin. Procedures Every other heifer calf born in each herd received the MAP vaccine; 162 vaccinates and 145 controls that had >= 1 lactation were included in analyses. Bacteriologic culture of fecal samples for MAP was performed annually for 7 years; results were confirmed via histologic methods and PCR assay. Production records and culture results were evaluated to determine effects of vaccination on variables of interest in study cows. Annual whole-herd prevalence of MAP shedding in feces was also determined. Results-Vaccinates had a significantly lower hazard of testing positive for MAP via culture of fecal samples than did controls over time (hazard ratio, 0.57; 95% confidence interval, 0.34 to 0.97). Fewer vaccinates developed clinical JD than did controls (n = 6 and 12, respectively), but these differences were nonsignificant. Overall within-herd longevity, total milk production, and calving-to-conception intervals were similar between vaccinates and controls. In all herds, prevalence of MAP shedding in feces decreased over time. Conclusions and Clinical Relevance-Vaccination with a killed whole-cell MAP vaccine appeared to be an effective tool as part of a program to control the spread of JD in dairy cattle. (J Am Vet Med Assoc 2013;242:663-669)