



**2013-05-03-039 Paratuberculosis databases updated (2013-05-02)**

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**New publications in the [PARATUBERCULOSIS database](#) (1422-1426)**

1422 Abendano, N., Sevilla, I.A., Prieto, J.M. , Garrido, J.M., Juste, R.A., Alonso-Hearn, M.

**Mycobacterium avium subspecies paratuberculosis isolates from sheep and goats show reduced persistence in bovine macrophages than cattle, bison, deer and wild boar strains regardless of genotype**

Veterinary Microbiology, (2013) 163, 325-334

Assessment of the virulence of isolates of Mycobacterium avium subsp. paratuberculosis (Map) exhibiting distinct genotypes and isolated from different hosts may help to clarify the degree to which clinical manifestations of the disease in cattle can be attributed to bacterial or to host factors. The objective of this study was to test the ability of 10 isolates of Map representing distinct genotypes and isolated from domestic (cattle, sheep, and goat), and wildlife animal species (fallow deer, deer, wild boar, and bison) to enter and grow in bovine macrophages. The isolates were previously typed using IS1311 PCR followed by restriction endonuclease analysis into types C, S or B. Intracellular growth of the isolates in a bovine macrophage-like cell line (BoMac) and in primary bovine monocyte-derived macrophages (MDM) was evaluated by quantification of CFU numbers in the initial inoculum and inside of the host cells at 2 h and 7 d p.i. using an automatic liquid culture system (Bactec MGIT 960). Individual data illustrated that growth was less variable in BoMac than in MDM cells. All the isolates from goat and sheep hosts persisted within BoMac cells in lower CFU numbers than the other tested isolates after 7 days of infection regardless of genotype. In addition, BoMac cells exhibited differential inflammatory, apoptotic and destructive responses when infected with a bovine or an ovine isolate; which correlated with the differential survival of these strains within BoMac cells. Our results indicated that the survival of the tested Map isolates within bovine macrophages is associated with the specific host from which the isolates were initially isolated. (C) 2013 Elsevier B.V. All rights reserved.

1423 VinodhKumar, O.R., Gunaseelan, L., Ronald, B.S.M., Sakthivelan, S.M.

**Slaughterhouse prevalence of ovine paratuberculosis in Southern India**

Tropical Animal Health and Production, (2013) 45, 1063-1069

Ovine paratuberculosis is a threat to small animal holders in terms of economic loss such as reduced growth performance and early culling. In order to study the slaughterhouse prevalence of ovine paratuberculosis, the slaughterhouse sheep samples (which are poor in body condition) collected over a period of two and half years from 1,034 suspected male sheep (poor in body condition) and 40 normal sheep (good body condition and subsequently negative by all the diagnostic tests employed) aged between 16 and 18 months were slaughtered at various abattoirs of Tamil Nadu. All the sheep taken in this study were maintained in almost same management conditions. DNA was extracted from 1,034 intestinal tissue and mesenteric lymph node and 121 were positive by IS 900 PCR. One hundred ten and 56 were positive by absorbed ELISA and Ziehl-Neelsen staining, respectively. In histopathology, 28 animals showed gross lesions of paratuberculosis infection (20-multibacillary and 8-paucibacillary forms). Out of 1,034 sheep tissues cultured, 32 showed cultural growth in Middlebrook 7H9 and 26 in Herrold's egg yolk medium. None of the 40 normal sheep were positive by any of the tests employed. In general, the mean body weight of



paratuberculosis-affected animal either by any one of the tests employed was less than the non-affected sheep. The approximate economic loss per sheep/farmer/year is around Rs 1,840 (US\$ 38.33) in paratuberculosis-affected sheep.

1424 Tirkkonen, T., Nieminen, T., Ali-Vehmas, T., Peltoniemi, O.A.T., Wellenberg, G.J., Pakarinen, J.

**Quantification of *Mycobacterium avium* subspecies in pig tissues by real-time quantitative PCR**

Acta Veterinaria Scandinavica, (2013) 55, Article Number: 26 DOI: 10.1186/1751-0147-55-26 Published: MAR 22 2013-

Background: Mycobacterioses in animals cause economical losses and certain *Mycobacterium avium* subspecies are regarded as potential zoonotic agents. The evaluation of the zoonotic risk caused by *M. avium* subspecies requires information about the quantities of *Mycobacterium* strains in infected animals. Because *M. avium* subspecies in pig tissues are difficult or even impossible to quantify by culturing, we tested the suitability of a culture-independent real-time quantitative PCR (qPCR) assay for this purpose. Methods: Mycobacterial DNA was extracted from porcine tissues by a novel method and quantified by *Mycobacterium* genus specific qPCR assay targeting the 16S rRNA gene. Results: The response of the qPCR assay to the amount of *M. avium* subspecies *avium* mixed with porcine liver was linear in the range of approximately log<sub>10</sub>(5) to log<sub>10</sub>(7) *Mycobacterium* cells per 1 g of liver. The assay was validated with three other *M. avium* subspecies strains. When the assay was applied to porcine lymph nodes with or without visible lesions related to *Mycobacterium avium* subspecies infections, around 10<sup>(4)</sup>-10<sup>(7)</sup> mycobacterial genomes per gram of lymph nodes were detected. Conclusions: The qPCR assay was found to be suitable for the quantification of *Mycobacterium avium* subspecies in porcine lymph nodes and liver.

1425 Desio, G., Nizza, S., Montagnaro, S., Sasso, S., De Martino, L., Iovane, V., Ciarcia, R., Casalnuovo, F., Pagnini, U.

**Estimated prevalence of Johne's disease in herds of water buffaloes (*Bubalus bubalis*) in the province of Caserta**

Italian Journal of Animal Science, (2013) 12, Article Number: e8 DOI: 10.4081/ijas.2013.e8 Published: 2013-

Paratuberculosis is a chronic infection of domestic and wild ruminants, caused by *Mycobacterium avium* subsp. *paratuberculosis*. The persistence of paratuberculosis infection for months up to years without exhibiting any clinical signs makes the diagnosis and control program a difficult proposition. Limited informations on prevalence of paratuberculosis in water buffaloes (*Bubalus bubalis*) are available. We carried out a study on 1350 buffaloes belonging to 56 herds in the Caserta province, of Campania region, Italy. The prevalence of infected buffalo dairy herds was estimated by a commercial ELISA kit of individual blood samples of animals over 24 months of age. On the basis of performance (sensitivity 43%, specificity 99.3%) of ELISA test on serum, the resulting true prevalence at animal level and at herd level was 4% (95% CI 3% to 5%) and 74,1% (95% CI 71.8% to 76%). Considering the paucity of epidemiological reports in the region our results could be a useful contribution towards the prevention of buffalo paratuberculosis in the area.

1426 Sikandar, A., Cheema, A.H., Younus, M., Zaneb, H.

***Mycobacterium Avium* Subspecies Paratuberculosis Multibacillary Infection (Johne's disease) in a Teddy Goat**

Pakistan Veterinary Journal, (2013) 33, 259-261

A 9-year old, debilitated, female teddy goat, with a body weight of about 23 kg, was subjected to smear staining, histopathological examination and ELISA for the diagnosis of Johne's disease (JD). During postmortem, the intestine showed thick corrugated mucosa and the mesenteric lymph nodes were found enlarged and edematous. Acid fast bacilli of multibacillary form were detected in Ziehl-Neelsen stained smears prepared from the tissues which showed gross pathology. Histopathologically, the ileal mucosa was intensely infiltrated by mononuclear cells and one of the ileum-associated lymph node revealed a large granuloma in its para cortical region. Special staining of tissue sections demonstrated the occurrence of acid fast



bacilli. The JD case was confirmed by using indirect ELISA. The present case was differed from the previously reported studies in two aspects viz 1) A confirmed case of multibacillary form of JD in a teddy goat 2) Unusual presence of a large granuloma in the lymph node. (C)2012 PVJ. All rights reserved To Cite This Article: Sikandar A, AH Cheema, M Younus and H Zaneb, 2013. Mycobacterium avium subspecies paratuberculosis multibacillary infection (Johne's disease) in a Teddy goat. Pak Vet J, 33(2): 259-261 PDF WILL NOT BE AVAILABLE..

**New publications in the [CROHN'S DISEASE AND PARATUBERCULOSIS database \(801-804\)](#)**  
801 Stevens, C., Henderson, P., Nimmo, E.R., Soares, D.C., Dogan, B., Simpson, K.W., Barrett, J.C., Wilson, D.C., Satsangi, J.

**The intermediate filament protein, vimentin, is a regulator of NOD2 activity**

Gut, (2013) 62, 695-707

Objective Mutations in the nucleotide-binding oligomerisation domain-containing protein 2 (NOD2) gene remain the strongest genetic determinants for Crohn's disease (CD). Having previously identified vimentin as a novel NOD2-interacting protein, the authors aimed to investigate the regulatory effects of vimentin on NOD2 function and the association of variants in Vim with CD susceptibility. Design Coimmunoprecipitation, fluorescent microscopy and fractionation were used to confirm the interaction between NOD2 and vimentin. HEK293 cells stably expressing wild-type NOD2 or a NOD2 frameshift variant (L1007fs) and SW480 colonic epithelial cells were used alongside the vimentin inhibitor, withaferin A (WFA), to assess effects on NOD2 function using the nuclear factor-kappaB (NF-kappa B) reporter gene, green fluorescent protein-LC3-based autophagy, and bacterial gentamicin protection assays. International genome-wide association meta-analysis data were used to test for associations of single-nucleotide polymorphisms in Vim with CD susceptibility. Results The leucine-rich repeat domain of NOD2 contained the elements required for vimentin binding; CD-associated polymorphisms disrupted this interaction. NOD2 and vimentin colocalised at the cell plasma membrane, and cytosolic mislocalisation of the L1007fs and R702W variants correlated with an inability to interact with vimentin. Use of WFA demonstrated that vimentin was required for NOD2-dependent NF-kappa B activation and muramyl dipeptide-induced autophagy induction, and that NOD2 and vimentin regulated the invasion and survival properties of a CD-associated adherent-invasive Escherichia coli strain. Genetic analysis revealed an association signal across the haplotype block containing Vim. Conclusion Vimentin is an important regulator of NOD2 function and a potential novel therapeutic target in the treatment of CD. In addition, Vim is a candidate susceptibility gene for CD, supporting the functional data.

802 Liu, G.W., Bi, Y.J., Wang, R.N., Wang, X.H.

**Self-eating and self-defense: autophagy controls innate immunity and adaptive immunity**

Journal of Leukocyte Biology, (2013) 93, 511-519

Autophagy (macroautophagy; "self-eating") is a degradation process, in which cytoplasmic content is engulfed and degraded by the lysosome. And, immunity is an important mechanism of the "self-defense" system. Autophagy has long been recognized as a stress response to nutrient deprivation. This will provide energy and anabolic building blocks to maintain cellular bioenergetic homeostasis. Thus, autophagy plays critical roles in regulating a wide variety of pathophysiological processes, including tumorigenesis, embryo development, tissue remodeling, and most recently, immunity. The latter shows that a self-eating (autophagy) process could regulate a self-defense (immune) system. In this review, we summarize the recent findings regarding the regulatory and mechanistic insights of the autophagy pathway in immunity. J. Leukoc. Biol. 93: 511-519; 2013.

803 Seminerio, J.L., Loftus, E.V., Colombel, J.F., Thapa, P., Sandborn, W.J.

**Infliximab for Crohn's Disease: The First 500 Patients Followed Up Through 2009**

Digestive Diseases and Sciences, (2013) 58, 797-806

The aim of this study was to assess the long-term usage patterns and safety of infliximab in



patients with Crohn's disease in clinical practice. The medical records of 492 unselected patients treated with infliximab at Mayo Clinic were reviewed and abstracted for demographic features, usage patterns, and adverse events. The patients received a median of seven infusions and had a median follow-up of 6.3 years. Twenty-eight patients (6 %) were lost to follow-up, 63 patients (13 %) had no clinical benefit, and 401 patients (80 %) had partial or complete response. Of the responding patients, 114 (28 %) received induction treatment only, 167 (42 %) received initial episodic treatment (62 switched to scheduled maintenance treatment of whom 32 [42 %] were still on infliximab at last follow-up), and 120 (30 %) received scheduled maintenance treatment (56 patients [32 %] still on infliximab at last follow-up). Three patients (0.6 %) developed septic shock and six patients (1.5 %) developed septicemia. One patient (0.2 %) developed *Mycobacterium avium* complex. Histoplasmosis occurred in three patients (0.6 %). The cumulative 10-year probability for developing cancer after infliximab was 9 %. Among the 31 patients developing malignancies (6 %), 15 (3 %) had solid tumors, 11 (2 %) had melanoma and non-melanoma skin cancers, three (0.6 %) had lymphomas (0.6 %), and two (0.4 %) had leukemia. Overall 10-year survival after the final course of infliximab was 94 %. Among the 28 deaths (6 %), nine occurred within 12 weeks of an infliximab infusion-two of these deaths were due to infections. Long-term follow-up of patients with Crohn's disease who were treated with infliximab initially between 1998 and 2002 showed persistence of therapy (due to clinical benefit) and an acceptable safety profile, despite the fact that less than one-third initially received three-dose induction followed by scheduled maintenance therapy. Infections and malignancy occurred at rates similar to those previously reported.

804 Berthelot, J.M., de la Cochetiere, M.F., Potel, G., Le Goff, B., Maugars, Y.

**Evidence supporting a role for dormant bacteria in the pathogenesis of spondylarthritis**

Joint Bone Spine, (2013) 80, 135-140

Spondylarthritis is still viewed as a reaction to infectious agents, as opposed to an infection by persistent bacteria, for several reasons: (a) an infection is considered proven only when the organism can be cultured; (b) no studies have identified dormant bacteria in the tissues targeted by spondylarthritis; (c) the bacterial persistence hypothesis has no therapeutic implications at the time being, since antibiotics are effective neither on dormant bacteria nor on the manifestations of spondylarthritis; and (d) the high prevalence of borderline disorders combining features of spondylarthritis and of psoriatic arthritis, or even rheumatoid arthritis (RA), would indicate a role for dormant bacteria in these last two diseases. However, recent data on dormant bacteria have rekindled interest in the bacterial persistence hypothesis. Dormant bacteria cannot be cultured, because they express only a small group of genes, known as the regulon, which includes genes for transcription factors that block the expression of the usual bacterial genes. Certain forms of cell stress, such as molecule misfolding, promote the entry of bacteria into a state of dormancy, which induces the low-level release by the host cells of cytokines such as TNF. Whether HLA-B27 misfolding facilitates the persistence of dormant bacteria within spondylarthritis tissue targets remains to be determined. If it does, then treatments that reactivate dormant bacteria might make these organisms susceptible to appropriate antibiotics and might therefore serve as useful adjuncts to nonsteroidal anti-inflammatory drugs and TNF alpha antagonists. TNF alpha antagonists rarely reactivate dormant bacteria, with the exception of *Mycobacterium tuberculosis*, which, together with metastatic cells, is the most extensively studied latency model to date. (C) 2012 Societe francaise de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.