

2013-03-24-010 Paratuberculosis databases updated (2013-03-20)

(04) Mycobacterial diseases; (12) Scientific Information, research and education; .

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New publications in the [PARATUBERCULOSIS database](#) (1359-1374)

- 1359 Magin, W.S., Van Kruiningen, H.J., Colombel, J.F. (2013)  
**Immunohistochemical search for viral and bacterial antigens in Crohn's disease**  
Journal of Crohns & Colitis, 7, 161-166

Background: Recent studies show that diseased intestinal tissues of patients with Crohn's disease (CD) contain obstructed lymphatics, granulomas, and tertiary lymphoid organs, representing responses to persistent antigen. Methods: Forty-seven tissue sections from 28 CD patients and 20 tissue sections from 17 control patients were studied. Tissues were immunostained with antibody directed against adenovirus, Epstein-Barr virus, herpes simplex virus I, parvovirus B19, Listeria monocytogenes, Escherichia coli, Clostridium perfringens, and Mycobacterium avium subspecies paratuberculosis. Results: There was no evidence of adenovirus, Epstein-Barr virus, parvovirus B19, or M. avium subsp. paratuberculosis in the tissues. Clostridia were positively stained in the mucus of 18.5% of CD patients versus 35.3% of controls and in the tissue of 11.1% of CD patients but in no controls. Immunoreactivity to listeria antibody occurred in the mucus of 3.7% of CD patients and in 5.9% of controls while it occurred in the tissue of 37.0% of CD patients and 29.4% of controls. E. coli occurred in the mucus of 48.1% CD and 64.7% controls and in the tissue of 18.5% and 5.9% respectively. Conclusions: Of the agents demonstrated in this search, none was located in granulomas or inflamed lymphatics. Finding the common gut microbes, E. coli and clostridia, in the mucus of patients and controls was not unexpected. The minor focal staining of E. coli and clostridia does not suggest a primary role for these pathogens in CD. Positive staining for listeria in patients and controls may very well represent cross reactivity rather than specific identification. (C) 2012 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved

- 1360 Bower, K.L., Begg, D.J., Whittington, R.J. (2013)  
**Tissue localisation of Mycobacterium avium subspecies paratuberculosis following artificially induced intracellular and naked bacteraemia**  
Veterinary Microbiology, 162, 112-118

Mycobacterium avium subspecies paratuberculosis (MAP) is the causative agent of Johne's disease or paratuberculosis, a chronic enteritis of ruminants. While Johne's disease is primarily expressed in the gastrointestinal tract, isolation of MAP from extra-intestinal tissues indicates that microbial dissemination via the haematogenous route may occur during the infection. This study examined the movement of peripheral blood mononuclear cells (PBMCs) infected with MAP and the dissemination of MAP following mycobacteraemia induced by IV inoculation over a time frame of 3 days. Viable MAP were detected in the peripheral blood by culture at 24, 48 and 72 h post IV inoculation in 3 of 4 sheep while a fourth sheep was blood culture positive at 24 and 48 h. Seventy-two hours following IV inoculation, MAP in tissues was unevenly distributed. MAP was predominantly distributed to the filtering organs, i.e. the lung, liver and spleen, however MAP was also isolated from lymph nodes, especially those draining the neck. MAP was not isolated from gastrointestinal tissues or lymph nodes, heart or kidney at 72 h following IV inoculation. The rapidity of localisation of MAP to tissues after onset of induced bacteraemia suggests that intermittent seeding into blood in natural infection would be sufficient to account for dissemination. (C) 2012 Elsevier B.V. All rights reserved

- 1361 Hanifian, S., Khani, S., Barzegari, A., Shayegh, J. (2013)  
**Quantitative real-time PCR and culture examination of Mycobacterium avium subsp paratuberculosis at farm level**  
Veterinary Microbiology, 162, 160-165

Mycobacterium avium subsp. paratuberculosis (MAP) causes Johne's disease in ruminants and may contribute to Crohn's disease in humans. The aim of this study was to determine the occurrence and quantity of MAP in cattle feces and milk in the Iranian context. In addition, we evaluated the effect of cattle age as well as farming system as risk factors contributing to MAP load. For this, a total sample of 373 consisting of 150 cattle feces (CF), 150 individual cow's milk (ICM), as well as 73 bulk-tank milk (BTM) was collected randomly and regardless of the cattle health status. The samples were assayed using F57 quantitative real-time PCR (qPCR) and culture method. According to the results of qPCR which was found similar to 10 times more sensitive than culture assay, MAP was detected in 68.66%



(103/150) of the CF, 12% (18/150) of the ICM and 52.05% (38/73) of the BTM samples. In contrast to the previous reports, the quantity of MAP in the BTM (2.03-5.97 log cfu/50 ml) was statistically ( $p < 0.01$ ) higher than the ICM (0.90-1.97 log cfu/50 ml). Data suggested a direct relation ( $p < 0.01$ ) between the cattle age and the quantity of MAP in the CF samples, while the relation was not statistically significant ( $p > 0.05$ ) for the ICM. In addition, MAP load in the BTM samples obtained from traditional farms was significantly ( $p < 0.01$ ) higher than that of the industrial ones, while the differences in CF and ICM was not significant ( $p > 0.05$ ). (C) 2012 Elsevier B.V. All rights reserved

- 1362 Dalton, J.P., Hill, C. (2013)  
**Survival of *Mycobacterium avium* subsp paratuberculosis in Synthetic Human Gastric Juice and Acidified Porcine Bile**  
Applied and Environmental Microbiology, 79, 1418-1420
- The bactericidal activities of synthetic gastric juice and acidified porcine bile on *Mycobacterium avium* subsp. paratuberculosis were assessed using propidium monoazide (PMA)-mediated quantitative reverse transcription-PCR, which allowed rapid relative quantitative analysis of viable *M. avium* subsp. paratuberculosis cells
- 1363 Abendano, N., Juste, R.A., onso-Hearn, M. (2013)  
**Anti-Inflammatory and Antiapoptotic Responses to Infection: A Common Denominator of Human and Bovine Macrophages Infected with *Mycobacterium avium* Subsp paratuberculosis**  
Biomed Research International, None, Article Number: 908348 DOI: 10.1155/2013/908348 Published: 2013-*Mycobacterium avium* subsp. paratuberculosis (Map) is the causative agent of a chronic intestinal inflammation in ruminants named Johne's disease or paratuberculosis and a possible etiopathological agent of human Crohn's disease (CD). Analysis of macrophage transcriptomes in response to Map infection is expected to provide key missing information in the understanding of the role of this pathogen in establishing an inappropriate and persistent infection in a susceptible host and of the molecular mechanisms that might underlie the early phases of CD. In this paper we summarize transcriptomic studies of human and bovine peripheral blood mononuclear cells (PBMC), monocyte-derived macrophages (MDMs), and macrophages-like cell lines in vitro infected with Map. Most studies included in this paper consistently reported common gene expression signatures of bovine and human macrophages in response to Map such as enhanced expression of the anti-inflammatory cytokines IL-10 and IL-6, which promote bacterial survival. Overexpression of IL-10 could be responsible for the Map-associated reduction in the expression of the proapoptotic TNF-alpha gene observed in bovine and human macrophages
- 1364 Masala, S., Cossu, D., Pacifico, A., MoliCotti, P., Sechi, L.A. (2012)  
**Sardinian Type 1 diabetes patients, Transthyretin and *Mycobacterium avium* subspecies paratuberculosis infection**  
Gut Pathogens, 4, Article Number: 24 DOI: 10.1186/1757-4749-4-24 Published: DEC 27 2012- Background: *Mycobacterium avium* subsp. paratuberculosis (MAP) is the cause of Johne's disease, an enteric granulomatous disease. Recently, MAP has been associated with different autoimmune diseases such as Crohn's disease, type 1 diabetes (T1D) and multiple sclerosis. Transthyretin (TTR) is a plasma transport protein for thyroid hormone and forms a complex with retinol-binding protein. Reduced TTR plasma levels in MAP infected ovines have been reported. TTR exerts also a functional role in the pancreas promoting insulin release and protecting beta-cells from death. Our objective was to identify a protein that could be used as a diagnostic marker of T1D for determining disease progression and monitoring at-risk patients. We postulate that serological TTR levels would be reduced in T1D MAP exposed patients. Our hypothesis is based on the observation of cases of T1D patients with decreased TTR levels beside the reduced TTR plasma levels in ovines with Johne's disease. We quantified the plasma protein levels of TTR in 50 people with T1D and 51 age-matched healthy controls (HCs) by means of enzyme-linked immunosorbent assays (ELISA). Findings: Our pilot study showed that plasma TTR levels were not significantly lower/higher in T1D Sardinian cases compared to the HCs. Conclusion: These preliminary data indicate that plasma TTR may not be a good candidate biomarker for T1D diagnosis and further studies to elucidate the possible link are needed
- 1365 Cossu, A., Ferrannini, E., Fallahi, P., Antonelli, A., Sechi, L.A. (2013)  
**Antibodies recognizing specific *Mycobacterium avium* subsp paratuberculosis's MAP3738c protein in type 1 diabetes mellitus children are associated with serum Th1 (CXCL10) chemokine**  
Cytokine, 61, 337-339
- Recently *Mycobacterium avium* subsp. paratuberculosis (Map) was associated to type 1 diabetes mellitus (T1DM). In this study we investigated for Map presence in children affected by T1DM compared to healthy children. A pool of 212 sera from T1DM children at onset was compared to sera from 57



healthy children for humoral immune response towards the Map specific protein MAP3738c by ELISA. Serum concentrations of CXCL10 (pro-Th1) and CCL2 (pro-Th2) chemokines were also measured in both sera pool. Results showed that T1DM children had a stronger seropositivity towards MAP3738c protein compared to healthy children. Data highlighted also the correlation between serum activity of T1DM patients towards the specific protein of Map and the increase of CXCL10 concentration if compared to non-diabetic subjects. In conclusion, an immune response to Map in T1DM patients at onset was observed and this may indicate a role of the bacterium in triggering or precipitating the disease. (C) 2012 Elsevier Ltd. All rights reserved

- 1366 Cossu, D., Masala, S., Sechi, L.A. (2013)  
**A Sardinian map for multiple sclerosis**  
Future Microbiology, 8, 223-232

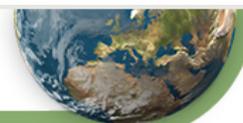
Multiple sclerosis (MS) is a complex autoimmune disease of the CNS. At present, MS etiology remains unknown, but it is believed to be caused by environmental factors acting on a genetic predisposition. Several studies suggest that different microorganisms could play a role in triggering autoimmunity, through immunological cross-reactivity or molecular mimicry. An overview of the knowledge regarding the bacteria involved in MS is given, placing emphasis on the newest candidate proposed: *Mycobacterium avium* subsp. *paratuberculosis*. This review will focus on discussing several arguments that might support a causal role for *Mycobacterium avium* subsp. *paratuberculosis* as an etiologic agent in MS. Additionally, a possible mechanism is postulated attempting to explain how the bacteria could initiate autoimmunity

- 1367 Karunasena, E., Kurkure, P.C., Lackey, R.D., McMahon, K.W., Kiernan, E.P., Graham, S., Alabady, M.S., Campos, D.L., Tatum, O.L., Brashears, M.M. (2013)  
**Effects of the probiotic *Lactobacillus animalis* in murine *Mycobacterium avium* subspecies *paratuberculosis* infection**  
Bmc Microbiology, 13, Article Number: 8 DOI: 10.1186/1471-2180-13-8 Published: JAN 16 2013-  
Background: MAP is a suspected zoonotic pathogen and the causative agent of Johne's Disease in cattle and other ruminant animals. With over \$ 1 billion dollars in loss to the dairy industry due to Johne's Disease, efforts to eliminate or reduce MAP from cattle are of importance. The purpose of this study was to determine if daily intake of probiotics could eliminate or reduce Johne's Disease associated symptoms and pathogenesis by MAP. Post infection, animals are often asymptomatic carriers with limited shedding of the pathogen, proving early detection to be difficult. Disease and symptoms often appear 3-4 years after infection with antibiotic treatment proving ineffective. Symptoms include chronic gastrointestinal inflammation leading to severe weight-loss from poor feed and water intake cause a wasting disease. These symptoms are similar to those found in individuals with Crohn's Disease (CD); MAP has been implicated by not proven to be the causative agent of CD. Probiotics administered to livestock animals, including dairy and beef cattle have demonstrated improvements in cattle performance and health. Our objectives included determining the benefits of *Lactobacillus animalis* (strain name: NP-51) in MAP infected BALB/c mice by evaluating systemic and gastrointestinal response by the host and gut microbiota. Male and female animals were fed 1x10(6) CFU/g probiotics in sterile, powdered mouse chow daily and infected with 1 x 10(7) CFU/ml MAP and compared to controls. Animals were evaluated for 180 days to assess acute and chronic stages of disease, with sample collection from animals every 45 days. MAP concentrations from liver and intestinal tissues were examined using real time-PCR methods and the expression of key inflammatory markers were measured during MAP infection (interferon-gamma [IFN-gamma], Interleukin-1 alpha, IL-12, IL-10, IL-6, and Tumor necrosis factor alpha [TNF-alpha]). Results: Our results demonstrate administration of probiotics reduces production of IFN-gamma and IL-6 while increasing TNF-alpha and IL-17 in chronic disease; healthful immune responses that reduce chronic inflammation associated to MAP infection. Conclusions: We observed that the immune system's response in the presence of probiotics to MAP contributes towards host health by influencing the activity of the immune system and gut microbial populations

- 1368 Sonawane, G.C., Tripathi, B.N. (2013)  
**Histopathological, Immunohistochemical and Molecular Studies of Naturally Occurring Paratuberculosis in Sheep**  
Journal of Comparative Pathology, 148, 52-52

Abstract not available.

- 1369 Vazquez, P., Garrido, J.M., Perez, V., Juste, R.A. (2013)  
**New Insights Into Immunopathological Forms of Bovine Paratuberculosis**  
Journal of Comparative Pathology, 148, 52-52



Abstract not available.

- 1370 Delgado, L., Guilloteau, L.A., Foret, B., Ferreras, M.C., Marin, J.F.G., Perez, V. (2013)  
**Cytokine and Inflammatory Mediator Expression in Intestinal Tissues of Lambs Showing Different Types of Lesions in Experimental Paratuberculosis**  
Journal of Comparative Pathology, 148, 80-80

Abstract not available.

- 1371 Fernandez, M., Sevilla, I., Benavides, J., Fuertes, M., Morales, S., Delgado, L., Garrido, J.M., Marin, J.F.G., Ferreras, M.C., Perez, V. (2013)  
**Lesional Immune Response in the Early Stages of An Experimental Infection of Lambs with Different Strains of Mycobacterium Avium Subspecies Paratuberculosis**  
Journal of Comparative Pathology, 148, 80-80

Abstract not available.

- 1372 Matos, A.C., Figueira, L., Martins, M.H., Matos, M., Andrade, S., Alvares, S., Mendes, A., Sousa, N., Coelho, A., Pinto, M.L. (2013)  
**Granulomatous Lesions and Mycobacterium Avium Subsp Paratuberculosis in Portuguese Wild Boars (Sus Scrofa)**  
Journal of Comparative Pathology, 148, 85-85

Abstract not available.

- 1373 Matos, A.C., Figueira, L., Martins, M.H., Matos, M., Pires, M.A., Alvares, S., Mendes, A., Sousa, N., Coelho, A., Pinto, M.L. (2013)  
**Diffuse Lymphadenitis and Disseminated Mycobacterium Avium Subsp Paratuberculosis Infection in Two Wild Eurasian Otters (Lutra Lutra L-1758)**  
Journal of Comparative Pathology, 148, 85-85

Abstract not available.

- 1374 Matos, A.C., Figueira, L., Martins, M.H., Matos, M., Pires, M.A., Alvares, S., Mendes, A., Sousa, N., Coelho, A., Pinto, M.L. (2013)  
**Renal Lesions in Deer (Cervus Elaphus): Involvement of Mycobacterium Avium Subsp Paratuberculosis**  
Journal of Comparative Pathology, 148, 85-85

Abstract not available.