

Does the bovine paratuberculosis pathogen play a role in the development of Crohn's disease in humans?

Joint communication No 022/2021 by the BfR and MRI from 15 July 2021

Mycobacterium avium subsp. *paratuberculosis* is known to cause so-called Johne's disease or paratuberculosis in cattle with a chronic inflammatory change in the small intestine.

Crohn's disease is one of the chronic inflammatory bowel diseases in humans and, along with ulcerative colitis, is the most important of these diseases. The cause of the disease is still unclear. The changes in the alimentary canal in Crohn's disease are similar to those observed in cattle paratuberculosis. This so-called pathognomonic similarity was one reason for the assumption that the pathogen causing paratuberculosis in cattle may be causally related to the development of Crohn's disease in humans.

The Federal Institute for Risk Assessment (BfR) and the Max Rubner Institute (MRI) carried out an extensive literature review and came to the conclusion that there are still no valid scientific results that prove such a connection.

Mycobacterium avium subsp. *paratuberculosis* (MAP) is a member of the genus *Mycobacterium* and is assigned to the so-called *Mycobacterium avium* complex. MAP is known to cause so-called Johne's disease or paratuberculosis in cattle. This infectious disease occurs in a large number of animal species. The disease is of particular and above all economic importance in ruminants such as cattle, goats and sheep that are kept as farm animals. Paratuberculosis is characterised by untreatable diarrhoea, as well as the associated emaciation and is always fatal. Pathologically, paratuberculosis manifests as a chronic inflammatory change in the small intestine featuring the typical folds resembling "cerebral convolutions". Similar changes can in part be observed in Crohn's disease (MC) in humans, which has led to the suspicion of a similar aetiology.

Crohn's disease is one of the chronic inflammatory bowel diseases in humans and, along with ulcerative colitis, is the most important of these diseases. The acute or chronic, intermittent and recurrent course of the disease can severely impair the patient's quality of life. The aetiology of the disease remains unclear, with autoimmune disease, genetic disposition, and infectious cause, and a combination of these factors being discussed.

The BfR has repeatedly dealt with the subject of MAP and its possible effects on human health, has published various statements and conducted expert discussions. A detailed literature study published in December 2003 by the BfR and the Robert Koch Institute on the subject of "Crohn's disease and *Mycobacterium avium* subsp. *paratuberculosis* (MAP)" concluded that there are no valid scientific results that prove a causal relationship between exposure to MAP and an increased risk of Crohn's disease. Subsequent opinions stated that a risk assessment regarding the importance of MAP and its intake through the consumption of food or water cannot be undertaken due to insufficient data.

The BfR and MRI carried out an extensive literature review on the level of knowledge of a potential connection between the pathogen causing paratuberculosis in cattle and Crohn's disease in humans with regard to the importance of food.

www.bfr.bund.de

The human studies carried out since 2003 on the importance of MAP in the development of Crohn's disease and a possible causal relationship do not provide any comparable results due to the heterogeneity of the selection of the methods and the study design. Many authors consider the evidence for a causal relationship to be insufficient, particularly due to the heterogeneous test results with regard to positive MAP detection in patients with Crohn's disease. It remains doubtful whether the MAP detection in patients with Crohn's disease, which is described in some studies and is more common than in control groups, indicates a causal role of the pathogen in Crohn's disease or whether it is rather a consequence of the disruption of the intestinal mucosal barrier in patients with Crohn's disease. There are a number of reasons for the latter interpretation. A role of MAP as a cofactor can be a possible effect in the development of Crohn's disease, although this is assessed as minor in comparison to other factors. In addition, the infection dosage for humans is presently unknown. It is not possible to provide information on the likelihood of occurrence and the type, duration, reversibility and severity of the possible health impairments in humans. However, discussion is still ongoing regarding the role of MAP as a causative agent for Crohn's disease.

There are still no systematic surveys of the occurrence of MAP in food. There are still no internationally recognised standard methods for the detection of MAP in food. Some of the methods used to examine food have either been adopted from the field of animal disease diagnostics and adapted, or they are non-validated, in-house methods. For the reasons mentioned, the data on the occurrence of MAP in food is insufficient and subject to great uncertainty and therefore no valid information can be provided on the prevalence and concentration of MAP in food.

For the reasons mentioned, the greatest uncertainties in any risk assessment are connected with exposure assessment. It is unclear whether there is any causal evidence between the ingestion of MAP and the occurrence of Crohn's disease. Although causal involvement of MAP in the development of Crohn's disease has not been proven with certainty, it is often recommended that consumer exposure to MAP in food be minimised as much as possible. This means reducing or preventing its entry into the food chain and into ready-to-eat foods as much as possible. In the dairy chain, for example, this means a consistent fight against Johne's disease, improvements in milking hygiene and the use of suitable process technologies to reduce germs. In addition, the BfR generally recommends against the consumption of raw milk and other raw animal products because of other pathogens, particularly for immunocompromised people.

Further information is available on the BfR website about Crohn's disease and *Mycobacterium avium ssp. Paratuberculosis*

Literature study of "Crohn's disease and *Mycobacterium avium ssp. paratuberculosis*":
https://www.bfr.bund.de/cm/343/morbus_crohn_und_mycobacterium_avium_ssp_paratuberculosis_literaturstudie.pdf

Expert discussion on the microbiological risk assessment of a connection between *Mycobacterium paratuberculosis* and Crohn's disease:
<https://www.bfr.bund.de/cm/343/protokollmcpa.pdf>



BfR 'Opinions app'

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. The BfR advises the Federal Government and the States ('Laender') on questions of food, chemical and product safety. The BfR conducts its own research on topics that are closely linked to its assessment tasks.