

Study: Multi-country bovine neonatal pancytopenia

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Figure: Healthy calves

Bovine neonatal pancytopenia (BNP) first emerged as a novel disease syndrome in 2007; initially in Germany, and soon afterwards in several other European countries including the United Kingdom, the Netherlands, France and Belgium. It affected calves aged less than one month and caused multiple unexplained external and internal haemorrhages, usually leading to death. There were a number of investigations into the possible cause of this new syndrome, but no infectious agents or poisons were found. Some evidence was found of an association between BNP in calves and vaccination of their dams against BVD using PregSure®BVD, (PregSure) manufactured by Pfizer Animal Health, so as a precaution the vaccine was withdrawn from the market in 2010. Reports of BNP were sporadic and incidence was very low, despite the widespread use of this vaccine in many European countries.

In 2010 a consortium of veterinary researchers from France (ONIRIS from Nantes), Germany (LMU from Munich), Belgium (Ghent University) and the Netherlands (Utrecht University and GD Animal Health) under the leadership of Prof. Dirk Pfeiffer of the Veterinary Epidemiology, Economics and Public Health Group at the Royal Veterinary College, London, conducted a case-control study to investigate [risk factors](#) for BNP at the level of the individual calf. This multi-country study recruited BNP-affected farms in France, Germany, Belgium and the Netherlands and used an interview questionnaire to gather data on the management of BNP case calves and matched healthy control calves from the same farm. Questions included the characteristics of the dam and sire, methods of feeding colostrum and milk, and dam vaccination history.

This study provided strong evidence that receiving colostrum from a PregSure-vaccinated cow is a major risk factor for BNP, but not the only one. If calves are only given colostrum from unvaccinated cows then it is highly unlikely they will develop BNP. The study did not identify any other important calf or management risk factors, suggesting that there are likely to be other important factors outside the scope of this study, such as the genotype of calf, dam and sire, that explain why BNP develops in only a small proportion of PregSure-colostrum-exposed calves. The study also found a small number of BNP [calves](#) (4.5% of cases) for which no association was found with either a PregSure-vaccinated dam or colostrum from PregSure-vaccinated dams. These could represent a background incidence of neonatal pancytopenia that is unrelated to ingestion of colostrum from PregSure-vaccinated dams.

Laboratory-based research into BNP pathogenesis is on-going by several other research groups. These groups have reported that BNP is associated with the presence of PregSure-induced maternal alloantibodies against the calf's bone marrow and blood cells, but there is debate about the specific antigens involved.

This study was funded by Pfizer Animal Health, the manufacturer of the implicated vaccine. Pfizer followed the implementation of the study but allowed the research team to conduct the study, and analyse and interpret the results independently. Conducting and co-ordinating a multi-country study was challenging due to differences in cattle production systems, and surveillance and laboratory systems between countries. Given this context, the collaborative spirit of the research team played a key role in bringing the study to a successful completion.

More information: Jones, BA; Sauter-Louis, C; Henning, J; Stoll, A; Nielen, M; Van Schaik, G; Smolenaars, A; Schouten, M; Ujil, I; Fourichon, C; Guatteo, R; Madouasse, A; Nusinovici, S; Deprez, P; De Vlieghe, SD; Laureyns, J; Booth, R; Cardwell, JM; Pfeiffer, DU. "Calf-level factors associated with bovine neonatal pancytopenia – a multi-country case-control study." *PLoS One* (2013), 8;12:e80619.

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