Enteric Immunity
Happy Gut, Healthy Animal

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KEYWORDS

• Bovine • Mucosal • Immunology • Enteric • Microbiome

KEY POINTS

- The largest organ of the immune system is the gastrointestinal (GI) mucosa, making the management of it essential for productivity and health.
- The barrier that consists of mucous, defensins, and immunoglobulin A is a "kill zone" to prevent microbial invasion of the GI epithelium.
- The enterocytes are key cells that maintain the "kill zone" and respond to metabolites and microbial components from the lumen and signals from immune cells to maintain tight junctions and prevent "leaky gut."
- Passive enteric immunity is essential for disease protection of the neonate; anti-inflammatory enteric response is essential disease protection for the growing and adult animal.
- Direct-fed microbials, including nutraceuticals, prebiotics, probiotics, and other dietary supplements, affect commensal "homeostasis" and mucosa immunity to maintain GI health.

INTRODUCTION

In the last decade, there has been an explosion of knowledge on the immune system with substantial implications for enteric health. This increase in knowledge revolves around the realization that the gastrointestinal (GI) tract is the largest immune organ of the body. It is understood that the mucosal immune system begins development in the fetus but does not become functional until epithelial cells of the mucosa in the neonate interact with microorganisms (microbiome) and/or their products in the gut lumen. The interaction between the epithelial cells and the microbiome is necessary for proper immune development, including immune system maturation, regulation, and maintenance of homeostasis. In this article, the interaction of immune system, microbiome, and the ability to maximize immunity are discussed.

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ONTOGENY AND ORGANIZATION OF ENTERIC MUCOSAL SYSTEM

The bovine mucosal immune system prevents bacterial invasion and shapes the gut microbiota, whereas the gut microbiota influences immune system development. The fetal calf is predominately protected by the innate immune system (**Fig. 1**).[1] The innate immune response of phagocytic cells (neutrophils and macrophages) does not fully develop until late gestation and declines before gestation because of fetal cortisol levels.[2] Humoral elements such as complement are present but are at levels below that of the adult. Interferon can be induced in the fetus as early as 60 days of gestation.[3] All of the cellular components of the acquired immune response are present in the fetal calf.[4] The number of peripheral blood T cells dramatically decrease, beginning 1 month before birth of the calf, as they traffic and populate lymphoid tissues of the fetal calf before birth (decrease ~60% to 30% at birth). B cells are much lower in the developing fetus (1%–2%).[4,5] The enteric mucosal lymphoid organ system begins developing at 100 days of gestation when the mesenteric lymph nodes are present (**Fig. 2**).[6–8] The continuous ileal Peyer patch (IPP) (see **Fig. 2**) becomes quite active by day 85 of gestation.[9] The B lymphocytes present are almost exclusively immunoglobulin M $(IgM)^+$ cells, and if the IPP are removed, the animals remain deficient in B cells for at least 1 year because the IPP is the major source of the peripheral B-cell pool.[9] Because the IPP is the site of both proliferation and negative selection, IPP follicles can be inferred as the major site for generation of the preimmune B-cell repertoire in ruminants,[8–10] whereas the discreet Peyer patches (PPs), distributed throughout the jejunum, function as induction sites for the generation of IgA plasma cells (see **Fig. 2**).[10] The role of the rumen in mucosal immunity is unclear because there are few leukocytes in the developing rumen. The first few weeks after birth are essential for long-term enteric immunity as the expression of host microRNAs (miR), and the presence of commensal microorganisms determines long-term gut and host health.[11] By day 21 of age, there is a maximum induction of host miR by high levels of microorganisms of the microbiome.[11] These immune developments include induction of

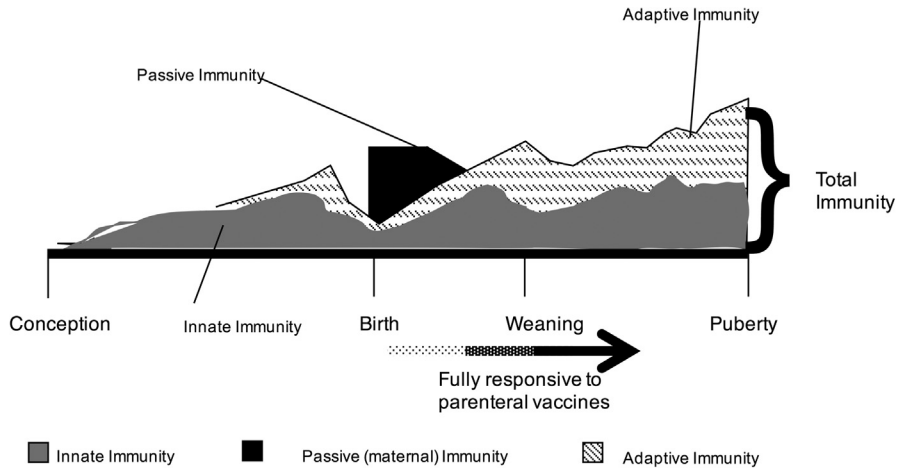

Fig. 1. Development of the immune response in the bovine: from conception to puberty. The calf's passive maternal immunity is only transferred after birth due to its unique placentation. (*Adapted from* Chase, Hurley DJ, Reber AJ, et al. Neonatal immune development in the calf and its impact on vaccine response. Vet Clin North Am Food Anim Pract 2008;24:88; with permission.)