E. coli and the protective role of Lactobacillus casei in newborn rabbits

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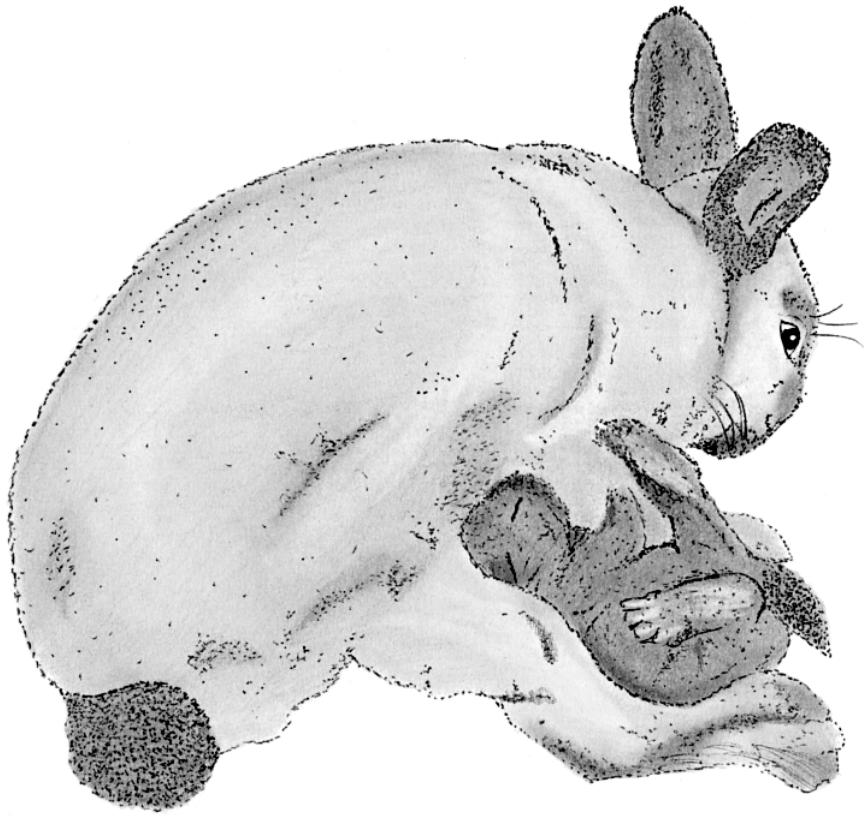
Newborn rabbits are unique in the animal world as their GI tract is, and remains absolutely devoid of bacteria during the first 3 weeks of their life. The absorbed milk has a pH of 5-6.5, which would enable bacteria to live, and colonize the gastro-intestinal (GI) tract. In the rabbit milk there is, however, one particular molecule (fatty acid) that prevents the survival of bacteria in the GI tract of the young rabbit. This molecule is sometimes referred to as "milk oil", and its production needs two parameters, milk of the mother and stomach of the suckling, to become active and hinder the development of bacteria.



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Pepe with her week old rabbit feeding

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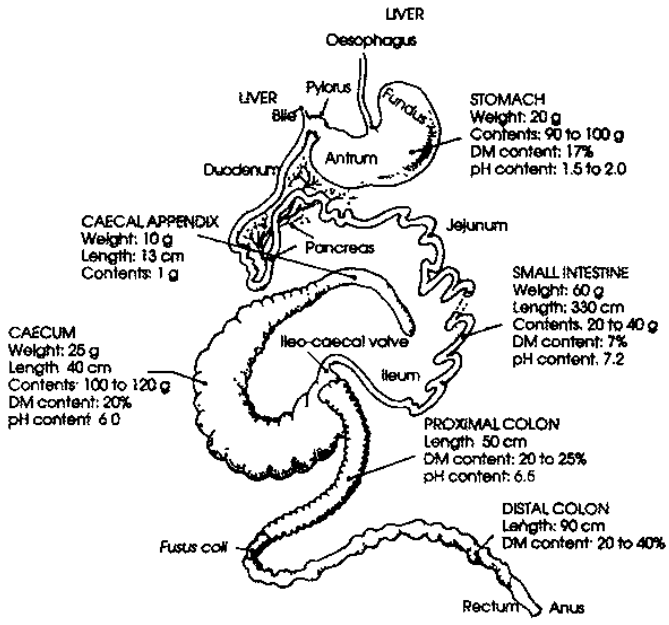
The digestive tract remains sterile during the first 3 weeks of the rabbit life. Passed that age, young rabbits have become strong, curious, leaves the nest, and nibble food that they find on their way naturally. Up to the 6th week of his life, a young rabbit will gradually decrease his milk intake, the concentration of milk oil in the stomach will decrease accordingly, and the pH of the stomach drops from about 5-6 to 1-2. Microorganisms that are ingested will survive the stomach passage, and start to grow/colonize rapidly in the cecum, and the different portions of the intestine. If the right bacteria are present, fermentation can start in the cecum.

This last phase is very important, and may go wrong. Indeed, microorganisms that develop inside the GI tract depend on the type of diet, hay, stress, etc, and it easily happens that pathologic bacteria colonize the sterile digestive tract. This leads to severe diarrhea and (fatal) enteric trouble.



Note: Numerical values are those observed in the New Zealand White breed, aged 12 weeks, fed a complete balanced pelleted feed.

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Gastro-intestinal tract of the rabbit

It is therefore important to keep the rabbits with the mother up to the age of 8 weeks, and not separate them earlier at 6 weeks or even younger. Once the complex microbial flora has colonized the GI tract, it will help prevent the development of pathologic bacteria. It is speculated food fermented by lactobacillus will help keep homeostasis between *Lactobacilli* sp., and other microbial flora of the GI tract, in animal species that host this bacteria naturally.

Orphaned rabbit babies fed on alternative source of milk does not develop this milk oil, and often show increased sensitivity to infections. One of the bacteria that cause fatal enteritis is *Escherichia coli*. A recent paper (2001, see ref in p.s. 2) discusses the protective role of *Lactobacillus casei*, a bacterium found in probiotic preparation such as Protexin, Probiocin,

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Benebac or Probios among others, against a toxin producing strain of *E. coli*.

This particular strain has been shown to cause hemorrhagic colitis (inflammation of the colon, accompanied by heavy bleeding), hemolytic-uremic syndrome (fever, acute renal failure, dissolution of red blood cells, and low number of platelet cells), and complications in the central nervous system. The mucosal damage in the GI tract is severe though not equal, and correlates with the number of observed pathogenic bacteria, and the concentration of the toxin: more pronounced in the cecum, and colon, less in the small intestine.

The study showed that most of the infected rabbits developed diarrhea quickly. Newborn rabbits treated with *L. casei* developed diarrhea too, but symptoms were less severe (16% severe diarrhea against 77.3% in the control group). The growth of the bacteria did not show a difference in both groups up to day 4 after infection; at day 7, the number of viable bacteria was 100 fold lower in the *L. casei* treated group. The same is observed for the toxin concentration: it remained stable after day 4 in *L. casei* treated rabbits.

Histopathologic examination of cecum, intestine, and colon showed that the control group suffered severe damage:

Small intestine:
- necrosis,
- vacuolation of epithelial cells.

Cecum:
- exfoliation of epithelial cells
- pseudo-eosinophil (type of white blood cell) infiltration,
- mitotic activity.

Colon:
- exfoliation of epithelial cells necrosis

None of the above pathology has been observed in *L. casei* treated rabbits.

The pH of the stomach and intestine are high in newborn rabbits, 5.1 and 6.5, respectively, and no differences were observed between the 2 groups. (Those high values probably help the *L. casei* bacterium survive the stomachal passage, and enable it to colonize the colon, cecum and large intestine of young rabbits.) The concentration of lactic acid was lightly higher in *L. casei* treated rabbits, as compared to the control group.

Interestingly, volatile fatty acids, like lactic acid, are known for their potent bactericidal activities, and are often added to the diet or to the water of weaning animals, in order to reduce the development of pathogenic bacteria.

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Lactic acid furthermore acts on the membrane of cells, affecting the rate of exchange of H^+ and Na^+ ions, the activity of the plasma membrane H^+/ATPase activities, and the fatty acid composition of the membrane. This leads to an acidification of the cytoplasm. In the case of this particular *E. coli* strain, it was shown that a concentration of 3.2 mM lactic acid was needed to inhibit its development, while less 1 mM was found in vivo. The presence of lactic acid thus may not explain the differences observed between the control, and *L. casei* treated group.

Lactobacilli and *Bifidobacilli* are moreover known to increase the secretion of *IgA* (immunoglobulin A or antibody that deactivates the activity of foreign bodies). This was observed in the newborn rabbits too. Higher levels of toxin present in a particular organ (i.e. colon) correlated to a higher the level of mucosal IgA present.

This study indicates that preventive administration of *L. casei* to newborm rabbits protects them from *E. coli* enteritis, by enhancing the secretion of specific *IgA*. Protection by its production of lactic acid is doubted in this case, since the in-vitro bactericidal needed 3 times higher concentrations.

Acknowledgements

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Further information

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