The impact of newborn nutrition on digestive tract development

Mother's Own Milk

Monika Słupecka studies mucosa development in the small intestines of newborn mammals and the role played by bioactive peptides found in the colostrum and milk

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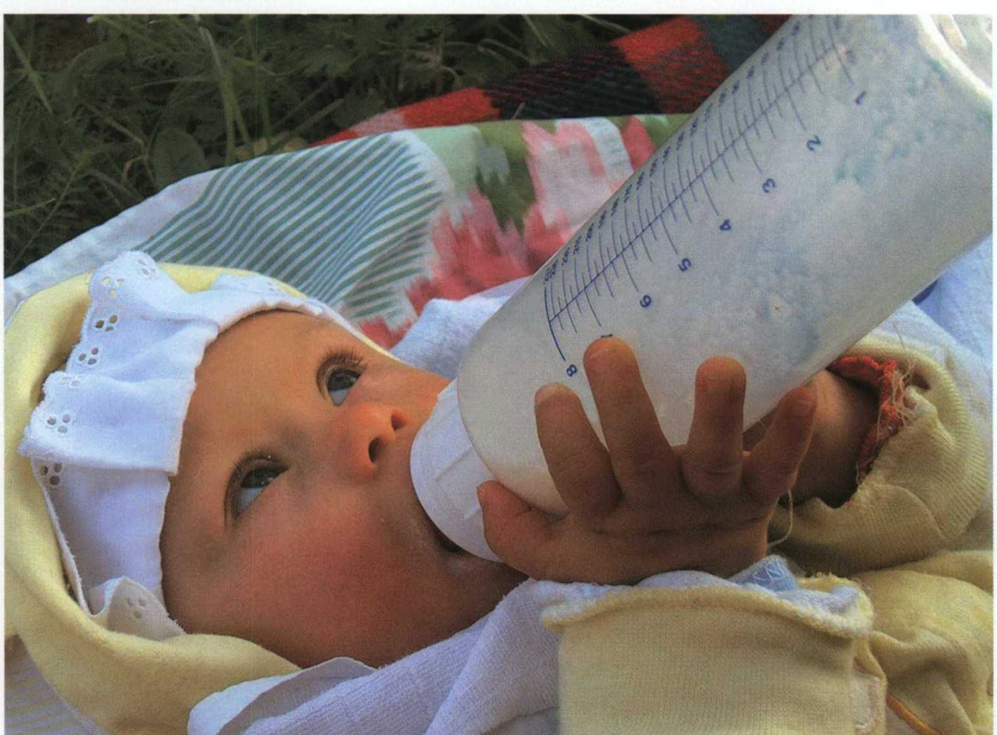
Newborn piglets offer the best model for studying mammalian gastrointestinal development, as their digestive tracts show many similarities to those of humans

Aside from pure scientific inquiry, research on neonatal development is motivated by such factors as complications observed in the perinatal period in humans and the high mortality rate seen among newborn farm animals. As experiments on human newborns are unethical and practically impossible, instead, *in vitro* screening studies (such as with cultured enterocytes) and *in vivo* studies using animals are widely carried out. The best model for studying the development of the mammalian gastrointestinal tract is found in newborn piglets.

Frequent diarrhea seen in newborns (especially dangerous in piglets) chiefly results from disturbances in the development and function of the digestive tract in the early post-natal period. The first half-day after a newborn mammal comes into the world poses a special challenge. Previously nourished by the placenta and protected against the ill effects of certain factors, a newborn has to immediately adapt to life outside the mother's body. From that moment onward, the young organism's own digestive tract (rather than the placenta) will be responsible for taking in and absorbing the food required for its further



Anna Cylonka, www.sxc.hu

The mystery of mammalian mother's milk lies in its content. Aside from nutritive ingredients, mammalian milk has been found to contain many biologically active substances development. The digestive tract begins to develop rapidly, in a process of trophic growth of organs and tissues combined with their functional maturation.

Starting off right

The first day of a piglet's life brings a 25% increase in stomach mass and a two-fold increase in hydrochloric acid secretion. The mass of the intestine increases by 70%, its length grows by 25%, and its width increases by 15%. The depth of the intestinal crypts increases and the intestinal villi grow longer.

At the same time, there is a significant upturn in the activity of enzymes - especially lactase, the enzyme responsible for digesting lactose, the main sugar in milk. Within the small intestinal mucosa, mitotic divisions in the stem cells of the intestinal crypts increase in number and the cells in the intestinal epithelium grow increasingly specialized: enterocytes are responsible for absorbing food components, goblet cells secrete intestinal mucuous, enteroendocrine cells are responsible for regulatory processes, nerve cells form part of the enteric nervous system (ENS), while Paneth cells play a part in immune processes.

Although the process of digestive tract development is genetically programmed, external factors such as diet, antinutritious substances, pathogens, and stressful conditions can exert a great impact on how it proceeds. In the early postnatal stage, a special role in the process of digestive tract growth and maturation is played by the newborn's first food - its mother's colostrum and milk. Colostrum (or foremilk) contains many bioactive substances, like immunoglobulins, enzymes, hormones, growth factors, and bioactive peptides, whose purpose is to guide digestive tract development. So far more than 20 bioactive peptides and proteins have been identified in colostrum and milk. They may be synthesized *de novo* by the mammary gland or extracted from the blood flowing through the gland. Some of these proteins and all of the peptides are secreted in biologically active form. Most of the milk proteins, called "nutritive" proteins (such as casein, lactoalbumin, lactoglobulin), are biologically inactive, but they serve as a source of active peptides produced within the digestive tract through their hydrolysis with the gastric and pancreatic juices. The concentration of most of the substances contained in colostrum or milk (including biologically active peptides and proteins) changes over the course of lactation. It is also species-specific. Biologically active peptides are an important trophic factor for the intestinal mucosa. They also affect the activity of intestinal and pancreatic enzymes, the intensity of cell division in the intestinal crypts and regulate the emptying of the stomach and intestinal contractile activity.

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Newborn piglets are the best model for studying digestive tract development in mammals

Absorbed without selection

Just after birth, a newborn's small intestine shows an ability for unselective absorption of substances of high molecular weight. This capacity, known as the open intestinal barrier, remains in effect for several hours or several days, depending on the species. It enables a newborn to absorb the immunoglobulins and regulatory proteins present in the colostrum. This phenomenon is particularly important in mammal species where, due to the structure of the placenta, the fetus is not supplied with immunoglobulins at the fetal stage (e.g. pigs, sheep, goats, cows). This deficiency is remedied just after birth through the absorption of immunoglob-

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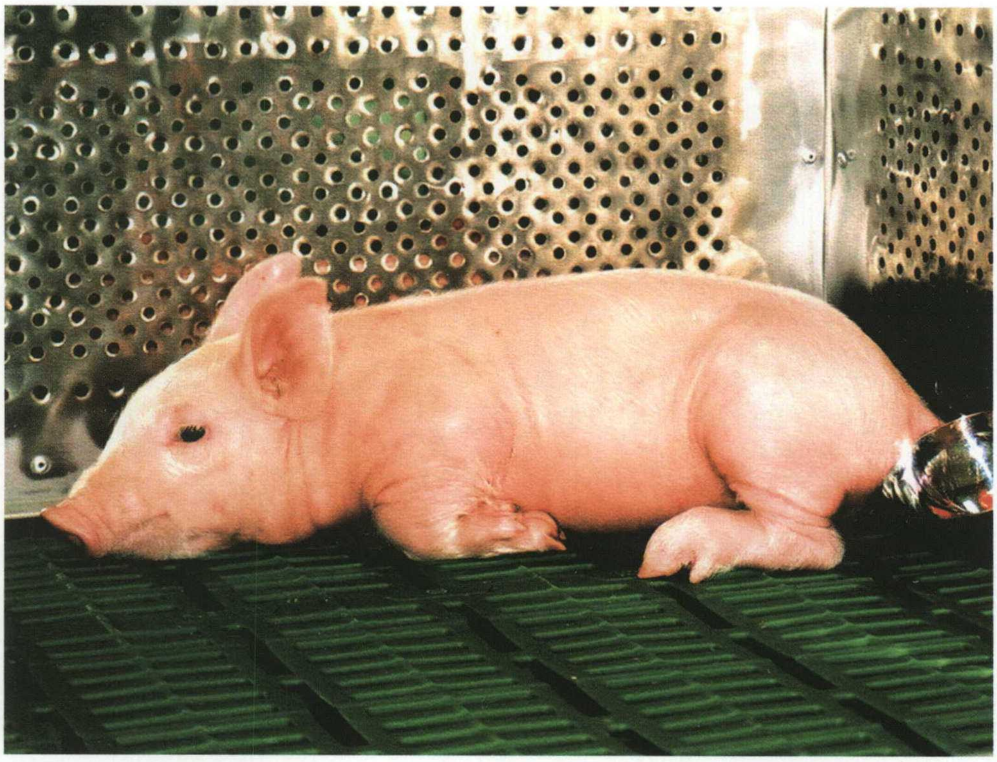

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Newborn piglets raised under laboratory conditions using an artificial sow feeding system

ulins from the colostrum. In other species, including humans, the survival of newborns does not hinge upon the supply of immunoglobulins in the colostrum. Nevertheless, the human small intestine is also capable of absorbing large-molecule substances, due to the existence of lysosomal vacuoles. Their presence in the enterocytes of a newborn baby's intestinal epithelium, and also their size, attest to the unselective process (via endocytosis) of substance absorption from the digestive lumen. This is important for the case of immune and regulatory proteins. Protein absorption is further facilitated by the presence of protease inhibitor in the colostrum.

A newborn's digestive glands, such as the salivary glands, stomach, and pancreas, are not yet capable of much secretory or enzymatic activity, a fact which helps keep active the immunoglobulins, hormones, and other bioactive factors in the colostrum and milk. The enzymes of the intestinal striated border do not evidence great proteolithic and lipolytic activity as compared to adult animals, and the utilization of food constituents is very high. The system of vacuoles in enterocytes plays an important role in the digestion of food constituents. The disappearance of intestinal-gland basal cells' ability to produce vacuoled enterocytes progresses along the small intestine at a species-determined time. This phenomenon is characteristic enough to serve as an indicator of the maturation of small intestinal mucosa function.

Straight from mom

Feeding on colostrum and milk leads to dynamic changes in the digestive tract. Piglets which suckle from their mothers during their first 24 hours of life have been shown to experience an increase in small intestine mass and size and increased DNA content in the mucosa, while such changes are not observed in piglets that are fed only water. Piglets feeding from their mothers have thinner intestines than those fed a 5% lactose solution. The protein content in the small intestinal mucosa was found to be significantly higher in piglets which received colostrum or milk, than in those fed with lactose.

A huge role in the development of the intestine is also played by whether colostrum is from the corresponding species. Piglets fed on sow colostrum from a bottle or colostrum from a different species (cow colostrum) show slower small intestinal mucosa development compared to piglets fed the same quantities of colostrum by natural means. Moreover, intestinal mucosa mass does not significantly differ between piglets that were fed sow milk from a bottle, cow milk, artificial milk formula, or water. The very act of sucking colostrum may cause an increase in protein synthesis in a piglet's enterocytes, and also increased concentration of RNA and DNA. Intensive intestinal mucosa growth is characterized by the rapid "replacement" of the epithelium cell population. Newborn animals (calves, piglets) fed with an artificial milk formula (based on cow's milk) saw a number of unfavorable structural changes in the intestinal mucosa, compared to those feeding on their mother's colostrum and milk. These differences suggest that a shortage or absence in artificial milk of biologically active and species-specific ingredients naturally present in colostrum and milk, e.g. IGF, insulin, lactoferin, and leptin, may have an adverse impact on a newborn organism. They cause a lower body mass, a slower process of epithelium cell replacement, lower protein content in mucosa, and also a shorter overall small intestine length.

The amount of food consumed also has an impact on small intestine development. Intestinal villi size, intestinal crypts depth, and mucosa width are seen to be significantly smaller in undernourished piglets.

Interestingly, not only the type and quantity of food, but also the way in which it is consumed affects intestine development. Piglets and rabbits deprived of contact with their mother and the ability to suckle do not evidence growth in intestine mass and size, or DNA content in the mucosa during their first day of life. Intestinal development was also found to be hampered in bottle-fed dog pups, even though their growth in body mass was identical to breast-fed pups. Piglets fed their own mother's milk from a bottle show complications in small intestine development not observed in breast-fed piglets: smaller intestinal crypt depth and smaller villi length, consequently causing significant narrowing of the mucosa.

Critical moment

The second critical moment in the life of a young mammal (after birth) comes with weaning, a process of shifting from suckling to solid food. This change in the type of food consumed and the stress caused by separation from the mother and experiencing new surroundings causes significant histological and biochemical changes in the stomach and small intestine, chiefly resulting from a drop in the intestine's digestive and absorptive capacity. The intestinal villi undergo atrophy, via either increased shedding of cells on the villi tips or reduced proliferation of cells in the intestinal crypts. The profile of enzymes in the striated border of the small intestinal mucosa changes significantly: the level of lactase lowers, while in reaction to substrates appearing in the intestinal lumen the levels of maltase and sucrase increase sharply.

The physiological processes taking place in the organism as it develops are very complex, making their study a difficult task. While the processes of digestive tract development can be influenced and altered, great caution does need to be maintained, especially in the case of young animals. ■

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Mucosa cells of the duodenum undergo cell death (apoptosis) at the tips of the intestinal villi

Further reading:

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