



Digestive physiology of rabbits in the pre- and post-weaning phases

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ABSTRACT. This review aimed to address all relevant parts of the digestive physiology of rabbits, before and after weaning, with a view to enabling greater understanding of these phases and reducing the mortality of kits. The biggest bottlenecks in Brazilian rabbit farming are linked to the period from birth to weaning, a time when the animals are more sensitive to environmental adverse events, requiring more rigid and efficient management due to their immune system being not fully developed. Throughout the period in which kits are with the females, many physiological changes occur, mainly in their gastrointestinal tract (GIT), which changes over time, depending on the type of food intake; in order to achieve its full capacity to utilize food, the intestine needs to undergo an adaptation from milk-based to solid diet. Thus, the digestive system in the intrauterine phase, in the nursing kits, and in the weaned babies will be covered. Therefore, understanding the physiology of baby rabbits proves to be of great value in reducing the mortality rate, so that management becomes more practical, providing producers with different problem-solving alternatives, in addition to greater profit.

Keywords: cecotrophy; rabbit farming; development; kits; gastrointestinal tract.

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Introduction

Despite its high growth potential in Brazil and around the world, rabbit farming is still in constant development. The biggest bottlenecks in Brazil are linked to the period from birth to weaning, a time when the animals are more sensitive to environmental adverse events, requiring more rigid and efficient management due to their immune system being not fully developed (Miranda & Castilha, 2020). Thus, ensuring good reproductive management increases the litter's chances of survival.

The control of reproductive management is very important so that there are kits to be sold, whether for meat production or even for breeding as companion animals, the so-called pet rabbits. Therefore, monitoring the entire gestation period of the breeders, the birth of the babies, and their development until weaning and after weaning becomes essential for better production and, consequently, increased financial return for rabbit farmers (Leite et al., 2022).

The females' gestation period lasts an average of 30 days; a few days before giving birth, the females remove their belly hair to make nests for the arrival of their kits, which is a way of keeping the latter hidden and helping regulate their body temperature. After birth, the kits depend solely on the female's maternal ability; they feed exclusively on breast milk until approximately 14 days of life (Blas & Wiseman, 2020; Machado et al., 2022), when they are already able to leave their nests and begin the transition to solid food (El Nagar, Sánchez, Ragab, Mínguez, & Izquierdo, 2014; Amroun, 2015) and to the cecotrophy processes (Sabatakou, Xylouri, Sotirakoglou, Fragiadakis, & Noikokyris, 2007).

Throughout the period in which the animals are with the female, many physiological changes occur in these animals, mainly in their gastrointestinal tract (GIT), so understanding said changes helps in the correct management of the animals, with beneficial consequences for the producer. In light of the foregoing, this review aims to address all relevant parts of the digestive physiology of rabbits in the pre- and post-weaning phases, with a view to enabling greater understanding of these phases and reducing the mortality of kits.

Development

Classified as non-ruminant herbivores (Irlbeck, 2001; Davies & Davies, 2003; Johnson-Delaney, 2006), rabbits are post-gastric or hindgut fermenters, characterized by having a digestive system with the caecum and colon, particularly the caecum, performing major functions in the digestion, absorption and utilization of nutrients, as well as in controlling digestive pathologies (Blas & Wiseman, 2020). Therefore, their GIT is adapted to digest large quantities of fibrous foods, with a strategy of high feed consumption and rapid intestinal transit, which guarantees them a good utilization of diets diluted in nutrients (Davies & Davies, 2003; Smith, 2014). However, in the stomach and small intestine, the digestion and absorption of nutrients by rabbits is very similar to that of other non-ruminant animals, or those considered monogastric animals (Smith, 2014).

An important point to be highlighted is that the GIT of rabbits changes over time, depending on the type of food intake; in order to reach its full capacity to utilize food, the intestine needs to undergo an adaptation from a milk-based to a solid diet (Blas & Wiseman, 2020), which occurs around 18 to 19 days of life, when kits already consume the food provided in the feeder (Davies & Davies, 2003; El Nagar et al., 2014).

Digestive system in the intrauterine phase

Just as in other mammalian species, the development of the digestive tract begins in the fetal phase of the rabbit and, at birth, the stomach and small intestine are the main components of their GIT (Blas & Wiseman, 2020). After birth, animals go from being in the uterus, where the mother meets all the needs of the fetus, such as breathing, metabolism, nutrient supply, excretion, defense against infections and pathogens through the placenta, to a new environment in which they become independent and need to keep performing all these functions on their own.

In order to continue receiving all the nutrients at rest, go through some adverse weather conditions, such as cold and heat, and still have nutritional supply for growth and development, kits begin to feed via the enteral route (mouth) and are affected by changes in the quantity and quality of the nutrients ingested (Alzina, 1997).

The gastrointestinal system has endocrine organs that are part of the immune system, carrying out the functions of digestion, absorption and secretion, being considered a tube that extends from the mouth to the anus (Mackie, 2002). After the embryo is fertilized, the digestive system undergoes some changes until it is complete, with its maturation finishing only after weaning, following six stages considering the main anatomical and functional events (Alzina, 1997).

The first stage in the development of the digestive system is organogenesis, which occurs shortly after the formation of the embryonic disc and is followed by the chemoarchitectonic phase of epithelial formation (stage two), which is responsible for the formation of the basic structure of the intestine. Soon after, the differentiation phase begins (stage three), which distinguishes epithelial cells from mesothelial cells (layer that internally lines the thorax, abdomen and the space around the heart). In stage four, called the maturation stage, the intestine begins preparations to handle extrauterine functions, after the rupture of the placenta and cutting of the umbilical cord. After these phases, birth occurs, initiating the neonatal stage (stage five), with the introduction of enteral feeding (milk for mammals); this process ends with the weaning phase (stage 6), characterized by transition from liquid to solid food (Alzina, 1997).

Considering that a rabbit's pregnancy lasts, on average, 30 days (Amroun, 2015; Klinger & Toledo 2018), it is possible to see the stomach glands from 26 days of gestation, with the villi and intestinal glands (crypts of Lieberkühn) being observable at 29 days of gestation (Sabatakou, Xylouri-Frangiadaki, Paraskevakou, & Papantonakis, 1999).

Digestive system in nursing kits

After birth, the intestine of the newborns is not yet complete, so in the first week of life, the Brunner's glands appear in the duodenum, and the morphology of the GIT is only complete after the kits are 20 days old, a point at which they no longer feed exclusively on breast milk (Blas & Wiseman, 2020).

It is worth mentioning that the hard feces that the female places inside the nest are also related to the good and rapid GIT development, since the baby rabbits, from birth, have contact with them, nibbling on them, which contributes to the pre-colonization of beneficial microorganisms from the GIT (Gidenne, Combes, Fidler, & Fortun-Lamothe, 2013). In addition to contact with them, which helps in the transition

phase from liquid food to solid food, with positive consequences in this process (Hudson, Cruz, Lucio, Ninomiya, & Martínez-Gómez, 1999; Kovács et al., 2006; Abecia, Fondevila, Balcells, & McEwan, 2007). Kacsala et al. (2018) state that this process can begin 2 to 3 days after birth. However, Combes, Gidenne, Cauquil, Bouches, and Fortun-Lamothe (2014) explained that the contact of the kits with the feces delays the development of the GIT, but the treatment without feces was the one with the highest mortality (9.5%) during the experimental period, which makes this a field of science that needs to be better studied.

Kovács et al. (2006) assessed the ingestion of feces from the mother by the babies; they distributed the animals into three treatments, all with eight kits per nest. The assessed treatments consisted of free access of the mother, with feces, to the nest, controlled breastfeeding, once a day and with free access to feces, and controlled breastfeeding, once a day and without access to feces, with breastfeeding lasting 20 to 30 min. As a result, they observed that the colonization of the caecum by bacteroid microorganisms begins 3 days after birth and that the size of the fecal pellets decreased in the nests of the treatments that contained this material, deducing that the baby rabbits ate it. However, the authors emphasize that maternal feces slightly influence the development of bacterial microflora, but that they do not play an exclusive role in colonization. Therefore, the development and colonization of the GIT may be faster depending on the type of environment in which the animals are housed, with or without contact with maternal feces.

The stomach of nursing kits has a gastric pH between 5 and 6.5, which is higher than that of animals that eat feed, which changes as it is ingested (Smith, 2014; Blas & Wiseman, 2020). The milk ingested by kits forms a sort of semi-solid curd in the stomach, which little by little passes into the small intestine to be digested and have its nutrients utilized; according to Henschel (1973), this is done by gastric proteases, mainly some different types of pepsins, which improves the efficiency of digestion by animals, as it increases the retention of material in the stomach.

During the breastfeeding period, the mucous glands secrete enzymes that digest the main components of milk, with gastric lipase being the major part of the lipolytic activity, which is also combined with the action of lactase until 25 days, as well as sucrase and maltase, which increase until 28 to 32 days of life. However, there is also proteolytic activity, but it decreases as it develops in the caecum, colon and pancreas (Blas & Wiseman, 2020). Soliman, Abdel-Razik, Hussein, and Rashad (2020) state that a rabbit's stomach is differentiated during embryonic life, with the gastric glands being functional during this period.

Unlike other mammalian species, in which the retention of gastric contents aims to increase the proliferation of bacteria, rabbits have protection against bacteria at this stage of life, called 'milk oil' – a type of antimicrobial fatty acid composed of octanoic and decanoic acid that prevents the kits from being contaminated at this stage –, in addition to maternal antibodies. This is due to the large amount of fat found in the female rabbit's milk – around 14%, together with the composition of the fat and the rabbits' enzymatic system, which makes their stomach and, consequently, their small intestine almost sterile (Cañas-Rodríguez & Smith, 1966).

Even with the 'milk oil' produced in the stomach, when the female's cecotrophs are consumed, because they are covered by a layer of mucin, the microorganisms present in them are able to remain intact until they reach the intestine and subsequently colonize it (Davies & Davies, 2003).

Abecia et al. (2007) state that, during the lactation period, the female's caecal microbiota positively influences the colonization of the kits' GIT. This can be explained by the establishment of the bacterial community in the first week of the baby rabbits' life, in which coliforms and *Streptococcus* spp. set in until 14 days of age, decreasing over time (*Streptococcus* spp.) or even disappearing (coliforms), while *Bacteroides* spp. increase after the first two weeks of the offspring's life (Kovács et al., 2006). However, fibrolytic bacteria (responsible for the hydrolysis of cellulose and other fibrous compounds) begin to colonize the caecum of rabbits after they start consuming solid food – around 15 days of life –, being absent before this period (Boulahrouf, Fonty, & Gouet, 1991).

Solid food consumption starts from 14 to 17 days of life (Amroun, 2015), with a gradual increase after 18 days (Beaumont et al., 2020). At 20 days, a rabbit's diet mostly consists of solid food, and the cecotrophy or cecotrophagy process (ingestion of soft pellets produced by partial fermentation in the caecum) begins. At 30 days, cecotrophy is fully developed, a point at which milk intake is minimal (Davies & Davies, 2003) and the animals can be weaned. However, in production systems, weaning between 28 and 45 days of life is common. Thus, it is during the feeding transition period that rabbits' GIT adapts and begins to be fully used, with enzymatic activities starting in the mouth and ending in the large intestine.

Oral cavity

Rabbits have a large visual field, with binocular vision of 10° to 35° in width and minimal overlap of visual fields due to the lateral positioning in the skull (Hof & Russell, 1977), which helps them perceive predators' movements. By tilting their head and moving their eyes upward, rabbits can reach a visual field of almost 360°, with the aid of their prominent globes, which extend up to 5 mm beyond the inferior orbital rim and 12 mm beyond the superior orbital rim, and of their large corneas (Peiffer Jr, Pohm-Thorsen, & Corcoran, 1994). This helps them be successful in escaping in nature while grazing, so their vision is not restricted to just the area below their noses, they have a broader view. Furthermore, rabbits have a visual range for green and blue colors (Juliussøn et al., 1994).

Therefore, the selection and subsequent ingestion of food happens through smell, with tactile recognition by the vibrissae, which are located around the nose and lips (Smith, 2014), with the upper lips being split (Davies & Davies, 2003). Their teeth are adapted to their eating habits and digestive physiology, suited to fibrous diets; they have two pairs of incisors, three premolars and three molars in the upper part, and one pair of incisors, two premolars and three molars in the lower part, totaling 28 teeth (Bertonnier-Brouty, Viriot, Joly, & Charles, 2020), as shown in Figure 1.

The incisor teeth are adapted for cutting food; rabbits have secondary incisor teeth just behind the main ones, with the lower ones staying behind the upper ones when they close their mouth, forming a kind of blade for cutting. Canine teeth are absent in rabbits; there is a wide diastema between the incisors and premolars. The premolars and molars, in their turn, are used to crush food before it is swallowed; they are called cheek teeth; rabbits can make up to 120 jaw movements per minute (Smith, 2014).

The chewing movement is divided into three stages, with the actions being type I (cutting with the incisors when grasping food), type II (chewing and crushing into smaller particles) and type III (formation of the food bolus for subsequent ingestion); with the exception of type II, in which only one side of the mouth is used at a time for the process (Davies & Davies, 2003). Primary teeth have limited growth, while permanent ones have continuous growth, requiring wear through food (Bertonnier-Brouty et al., 2020).

The process of food digestion by rabbits begins in the mouth, with constant secretions of saliva; these animals have four main pairs of salivary glands, namely parotid, mandibular, sublingual and zygomatic (Davies & Davies, 2003), which also have the function of moistening, lubricating the food bolus, and providing water to reduce its osmolarity (Reece, 2017). Figure 2 shows a rabbit's entire GIT, as well as the main salivary glands.

Chauncey, Henriques, and Tanzer (1963) found activities of the acid phosphatase, esterase and β -galactosidase enzymes, as well as large amounts of α -amylase in the saliva produced by the parotid and mandibular glands of rabbits. Lipase and urea are present only in small quantities, but the bicarbonate and potassium ions are also part of the secretions (Davies & Davies, 2003).

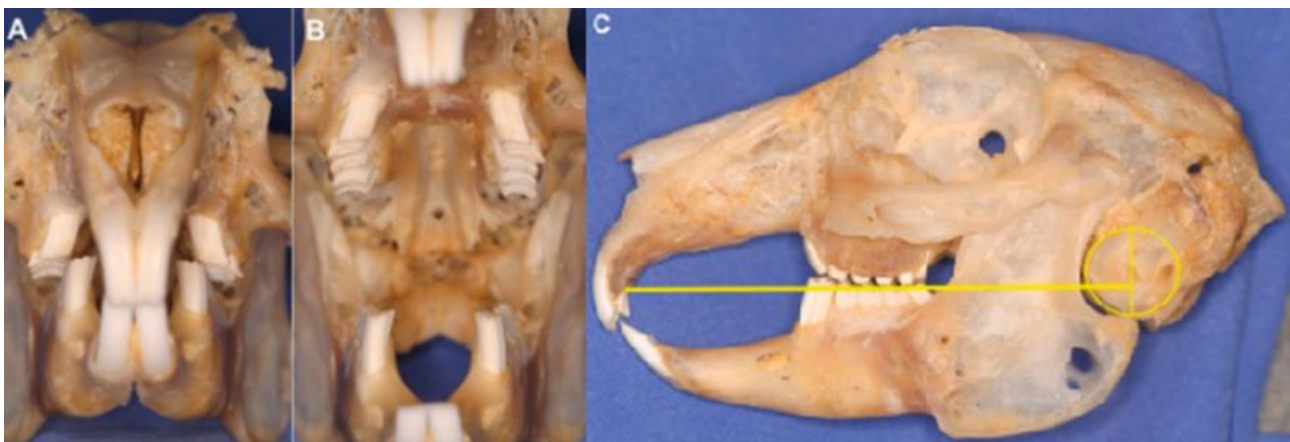


Figure 1. (A) Rostrocaudal view of an apparently healthy dentition in a pet rabbit with the mouth closed and (B) open. (C) Lateral view of the skull, with anatomical reference lines applied in accordance with Böhmer (2015) and Crossley (2003). The yellow line begins at the rostral end of the hard palate, immediately caudal to the second incisor, and extends caudally to pass through the tympanic bulla for approximately one-third of its height. In healthy pet rabbits, it marks the physiological occlusal plane between the upper and lower molars (Böhmer & Böhmer, 2020).

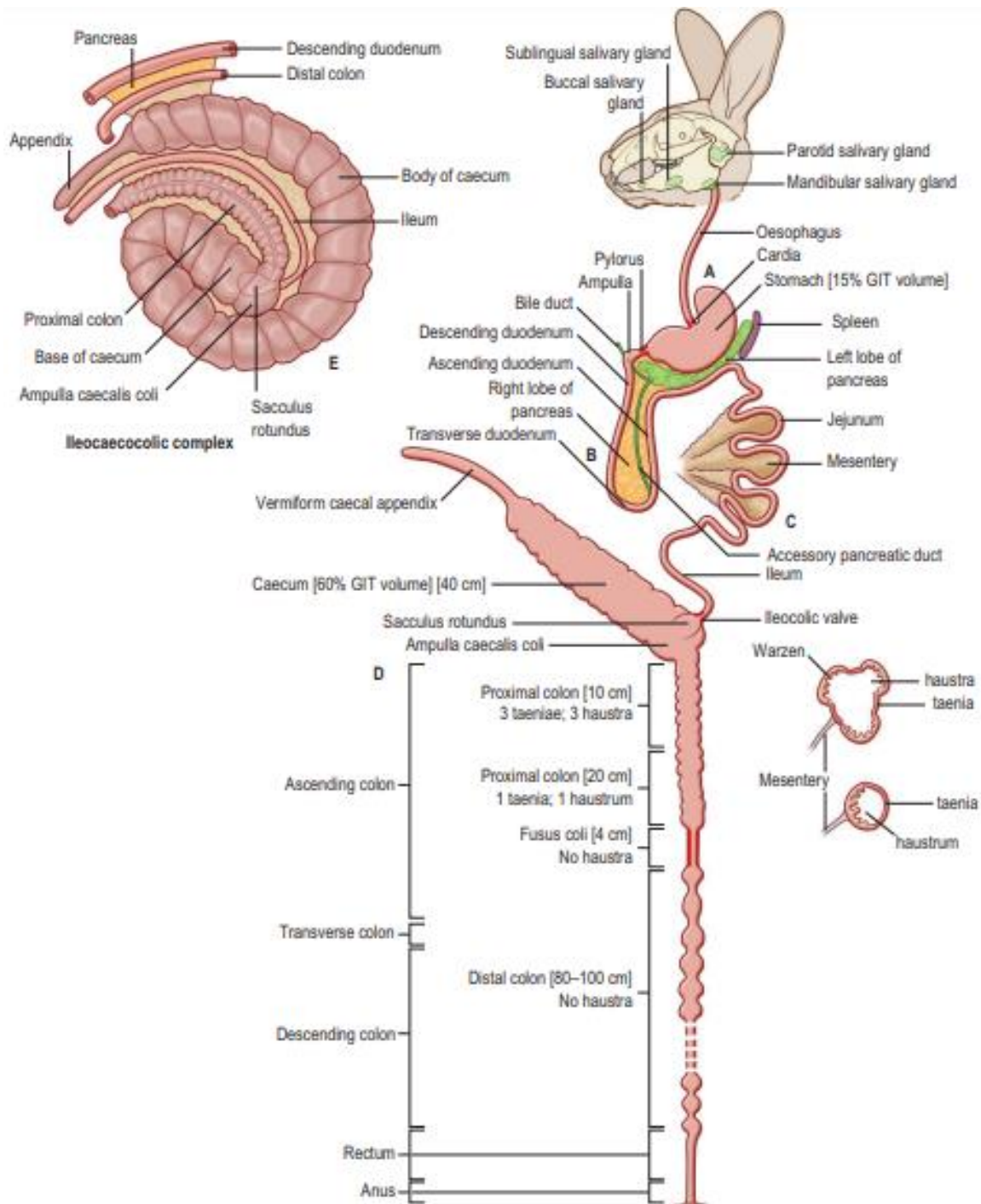


Figure 2. Schematic diagram of the anatomy of a rabbit's alimentary tract. (A) Oral cavity and stomach, (B) Portion of the small intestine called the duodenum (C) Portions of the small intestine called jejunum and ileum, (D) Portions composing the large intestine, such as caecum, colon and rectum, (E) Ventral view of the ileocaecocolic complex (Smith, 2014).

Esophagus

After passing through the oral cavity, food goes to the esophagus, an organ whose function is to propel food into the stomach. It consists of a two-layer muscular tube, lined in the lumen by stratified squamous epithelium (Orlando, Bryson, & Powell, 1984). The esophagus is an organ dependent on extrinsic vagal innervation, in which swallowing occurs through control of the brain stem, through vagovagal reflexes, having enteric ganglia and functioning as a network of local neurons to control motility (main function). At its ends, there are two sphincters – lower and upper esophageal sphincters –, which help with swallowing (Neuhuber, Raab, Berthoud, & Wörl, 2006). During food digestion, the esophagus has little or no effect on the process (Davies & Davies, 2003). Furthermore, peristalsis in the esophagus is virtually non-existent, with the food bolus being sent to the stomach by pressure (Klinger & Toledo, 2018).

Stomach

After passing through the esophagus, food goes to the stomach, considered an organ of fundamental importance for the food digestion process, comprising around 15% of the volume of a rabbit's GIT and being an organ that is never empty.

It is divided into three parts, namely cardia, fundus and pylorus (Madge, 1975). The cardia has invaginations in the submucosa, and simple and columnar epithelial cells, with the function of secreting mucus and working as buffer (Dukes, 2017). It has a thinner membrane compared to other mammalian animals, with a well-developed cardiac sphincter, which prevents the digesta from returning to the oral cavity, so that these animals do not regurgitate or have episodes of emesis (vomiting) (Davies & Davies, 2003; Smith, 2014).

It is in the fundic region that the main secretions of the stomach occur; it has parietal cells that secrete intrinsic factor and gastric acid, and peptide cells, responsible for the secretion of pepsinogen and renin in kits (Davies & Davies, 2003; Dukes, 2017). There is also constant secretion of mucus, with a protective function against acids and proteolytic enzymes.

In the pyloric region, there are deep glands lined with epithelial cells, which are responsible for the production of mucus and buffer, in addition to enteroendocrine cells, which produce hormones to help control the production of acid and proteolytic enzymes. Still in this last portion, there is the pyloric sphincter, which has the function of controlling the rate of passage of chyme to the duodenum (Reece, 2017).

The pH, after 20 days of a rabbit's life, begins to decrease, becoming more acidic (pH of an adult animal around 1-2), keeping the rabbit's stomach and, consequently, small intestine free from harmful microbial colonization (Davies & Davies, 2003). The passage of digesta varies between 3 and 6 hours (Smith, 2014); in addition to digesting food, the stomach has the function of regulating metabolic homeostasis and providing immunological defense (Soliman et al., 2020).

Small intestine

Upon leaving the stomach, the chyme passes to the small intestine; it is divided into three portions – duodenum, jejunum and ileum –, which begin the process of absorption of nutrients from food. It is approximately 3 meters long and is responsible for secreting bile, digestive enzymes and buffers (Blas & Wiseman, 2020). In this portion of the GIT, the pH is higher, around 7. However, Zanato et al. (2009) report pH values of 6.67; 7.43 and 7.37 for each portion, respectively – duodenum, jejunum and ileum.

The organ has four layers, namely: a) serous tunic, which covers it externally, composed of squamous epithelium cells over loose connective tissue; b) muscular tunic, composed of two layers, one of internal circular smooth muscle, and the other of external longitudinal smooth muscle; c) submucosa, and d) mucous tunica, the innermost layer of the small intestine, with projections into the lumen called villi, and invaginations into the mucous layer called crypts (crypts of Lieberkühn), both composed of simple columnar epithelium (Reece, 2017).

In the villi present in the mucous layer, microvilli are found, which, just as villi, have the function of expanding the area of contact with the chyme, increasing digestion and absorption of nutrients by the animal, being larger in the jejunum and smaller in the ileum (Smith, 2014; Reece, 2017). However, it is in the submucosal layer that Brunner's glands are present; located in the duodenum, they are responsible for alkalizing the chyme that comes from the stomach, since the intestine does not have an acidic pH, requiring buffering (Reece, 2017).

There are six types of cells in the crypts, namely: stem cells (mainly secrete mucus), enterocytes (secrete chloride, sodium and water into the lumen of the crypt), goblet cells (secrete mucus), enteroendocrine cells (function of monitoring pH, osmolarity, composing the ingesta in the lumen, and secreting hormones), Paneth cells (antibacterial protection function) and M cells (immune system cells). However, three types of cells are also found in the villi: the cells of the absorptive enterocyte (produce enzymes for the final digestion process and transport proteins for nutrients), goblet cells (produce mucus) and M cells (same function in crypts) (Reece, 2017).

Contents from the pancreas, liver and bile are secreted in the duodenal portion, each with an important function in the food digestion process. A rabbit's pancreas is relatively small, as its protein and carbohydrate intake is low. The main duct leads into the end of the duodenum and plays an important role in the secretion of trypsin, chymotrypsin, carboxypeptidases, amylase, several lipases, and bicarbonate ions (Davies & Davies, 2003). It is important to highlight that some secretions only become active when secreted in the duodenum, which is a way to prevent self-digestion in the duct (Reece, 2017).

The liver is one of the accessory organs of the GIT; its secretions occur in the form of bile, being extremely necessary for the digestion and absorption of fats. Moreover, it is responsible for processing nutrients transported by the blood, such as carbohydrates and proteins, for generating energy through lipids to be directed to the body's various metabolic pathways, for detox through biotransformation and excretion through bile to be eliminated along with feces, in addition to storing fat-soluble vitamins and sheltering Kupffer cells (protect the liver against bacteria) (Schinoni, 2006; Reece, 2017).

It is through the bile duct, which leads into the opening of the duodenum, that the liver performs its secretions; the bile produced by rabbits amounts to around 100 to 150 mL kg⁻¹ of BW, secreting some acids such as cholic and chenodeoxycholic acids, in addition to pigments (bilirubin and biliverdin). However, in rabbits, most of it is found as unconverted biliverdin, since the activity of the biliverdin reductase enzyme is low (Davies & Davies, 2003).

The jejunum is the longest portion of the small intestine, with the products from the digestion of the duodenum and jejunum being absorbed in this portion, such as monosaccharides and amino acids, through the brush border present in this region. The ileum also plays an important role, being responsible for regulating and recycling electrolytes that reabsorb bicarbonate ions to be reused by the body (Davies & Davies, 2003). However, the transit time of chyme in the small intestine varies in each portion, being very fast in the duodenum, and 10-20 and 30-60 minutes in the jejunum and ileum, respectively (Smith, 2014; Blas & Wiseman, 2020). However, the small intestine is the region of the GIT that has the greatest activity in the digestion and absorption of nutrients, through passive or active mucosal transport (Blas & Wiseman, 2020).

At the end of the ileum is the *sacculus rotundus*, an exclusive region of the small intestine of rabbits; it is a sphere-shaped enlargement with thick walls, composed of lymphoid tissue, forming the junction between the ileum, caecum and proximal colon (Smith, 2014; Wang, Huang, Wang, Liu, & Wang, 2020). This portion of the small intestine has immune, digestive and secretory functions (Wang et al., 2020). The digesta that passes from the ileum to the *sacculus rotundus* is controlled by an ileocolic valve, which also prevents it from returning to anterior portions of the small intestine (Smith, 2014). Furthermore, rabbits are a well-developed species in terms of lymphoid tissues compared to other mammalian species, as said tissues are also found in their Peyer's patches, caecal plates and vermiform appendix (Wang et al., 2020).

Large intestine

Integrated by the caecum, colon and rectum, a rabbit's large intestine is adapted for fermentation of dietary fiber, being the GIT region that helps increase the utilization of nutrients. However, it is through the *sacculus rotundus* (final portion of the ileum) that the digesta reaches the large intestine; the latter opens into the *ampulla cecalis coli*, forming a T-junction between the ileum, caecum and colon, with this region being efficient in separating and mixing what remains of digestion from the small intestine.

Large indigestible fiber particles are sent directly to the colon, while small particles and fluids are sent to the caecum in order to be fermented by microorganisms (Smith, 2014). The mucous tunic of this region has crypts, but not villi, being lined mainly by goblet cells, which secrete mucus, as well as absorptive epithelial cells, with the function of absorbing electrolytes and water (Reece, 2017).

A rabbit's caecum is lined by large layers of lymphoid tissue, but this region has a thin wall, whose epithelium presents goblet cells between tall columnar cells (Snipes, 1979), ending in a blind bottom called vermiform appendix. Proportionally to the size of a rabbit, its caecum is considered the largest among mammals, accounting for approximately 40 to 60% of the total volume of the GIT (Davies & Davies, 2003). However, it folds into four turns, the first three of which are made up of thin, translucent walls, and the fourth turn is made up of the vermiform appendix, which has a large amount of lymphoid tissue and the function of secreting bicarbonate ions, into the lumen of the caecum, to buffer volatile fatty acids (VFAs) produced during caecal fermentation (Davies & Davies, 2003); it can measure 13 to 14 cm in 4-month-old rabbits.

According to Dasso, Obiakor, Bach, Anderson, and Mage (2000), the vermiform appendix is rich in B cells and begins its development shortly after birth, which is driven by microorganisms present in the GIT. Moreover, it maintains its immune function throughout the rabbit's life, decreasing (but not ceasing) after adulthood.

The pH of a rabbit's caecum changes depending on feeding pattern, but, on average, it has a pH value of 6 (Fortun-Lamothe & Gidenne, 2006), varying according to the time of day, being more acidic in the middle of the afternoon, ranging between 5.9 and 6.8 (Davies & Davies, 2003). However, the caecum functions as an anaerobic chamber, which, like in all herbivores, degrades substrates through microorganisms. The latter, in their turn, produce VFAs that are then absorbed, having a symbiotic relationship with rabbits that provides a

favorable environment for microorganisms to maintain themselves. This large ecosystem plays an important role in a rabbit's digestive health, as well as in its immune status (Gidenne et al., 2008).

There are several microorganisms in the caecum of rabbits. In this sense, Crowley et al. (2017) assessed the composition of this environment and found several phyla, such as *Actinobacteria*, *Bacteroidetes*, *Fibrobacteria*, *Firmicutes*, *Proteobacteria* and *Tenericutes*, but no type of *Fibrobacteres* was identified, which are responsible for the degradation of the fiber, indicating that they are not the only ones responsible for this function. Velasco-Galilea et al. (2018) present the main genera of microorganisms in the caecum of rabbits, namely *Clostridium*, *Anaerofustis*, *Blautia*, *Akkermansia*, *rc4-4* and *Bacteroides*. However, the fibrolytic activity of bacteria begins after ingestion of solid foods, such as pectinolytic, xylanolytic and cellulolytic activity, and includes yeast (*Saccharomycopsis guttulatus*); in the adult stage, only strict anaerobic bacteria remain (Gidenne et al., 2008). Even so, there are several ciliated and flagellated protozoa, such as *Eutrichomastix* spp., *Enteromonas* spp., *Retortamonas* spp., and *Entamoeba cuniculi* (amoeboid organism) (Davies & Davies, 2003; Smith, 2014).

In addition to VFAs, with the fermentation of carbohydrates and amino acids, some gases are also produced, such as CO₂, CH₄ and H₂, in addition to ammonia (NH₃); VFAs supply 30 to 50% of the maintenance energy of rabbits, with highlight to acetate (60 to 80%), butyrate (8 to 20%) and propionate (3 to 10%), which are absorbed by the wall of the caecum and colon, falling into the bloodstream for utilization as a source of energy (Gidenne et al., 2008; Smith, 2014; Deblas & Wiseman, 2020). Figure 3 shows the fermentation process and nutrient metabolism in a rabbit's caecum, and the end products.

The *ampulla cecalis coli*, which is found in the caecum, is an important connecting region between the caecum, colon and ileum. It is the most muscular portion of the caecum, formed by open crypts lined with a mucous membrane, which, in its turn, has high columnar epithelium and few goblet cells (Snipes, 1979).

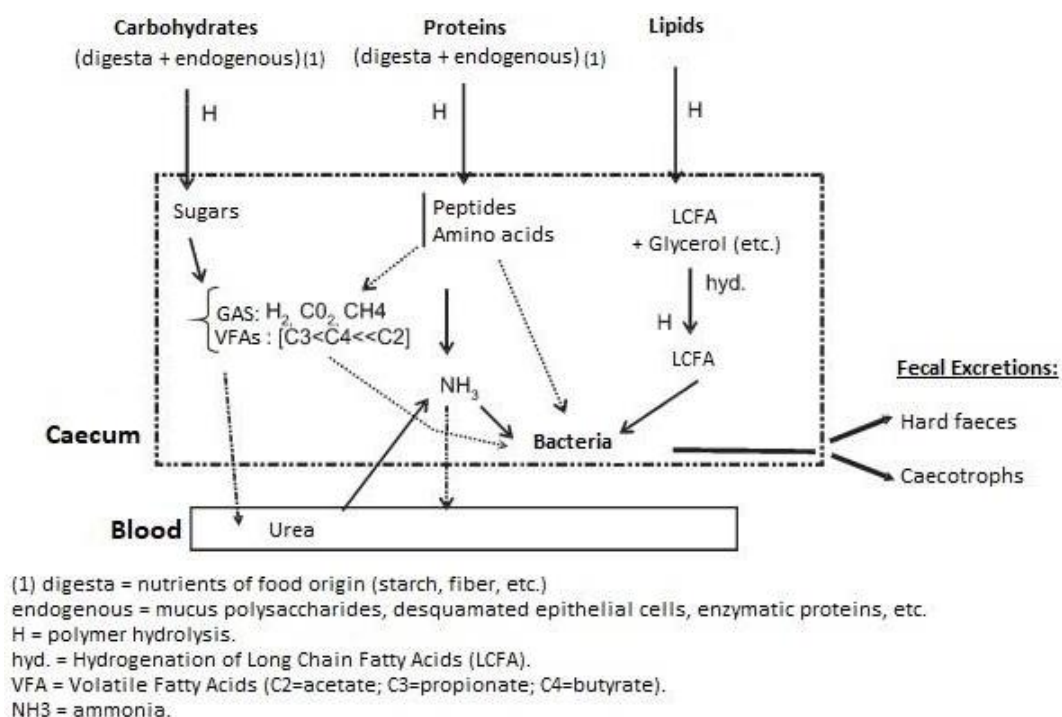


Figure 3. Caecal metabolism of the main nutrients and formation of microbial fermentation end products (Adapted from Gidenne et al., 2008).

The colon is the second portion of the large intestine, being divided into three regions: ascending, transverse and descending colons. The ascending colon is the longest and is divided into four members separated by flexures, formed by taenia and haustra (sacculations); the first member has three taenia and three haustra, the second, one taenium and one haustra, and the rest does not have it; the third member is called *fusus colli*, and the fourth, a muscular spacing in the region, which is exclusive to lagomorphs.

The *fusus colli* divides the colon into two parts, the proximal and the distal, as shown in Figure 2. It is worth mentioning that it is in this portion that the material that will be surrounded by mucus (cecotrophs) is separated from that which will not, in addition to functioning as a pacemaker to differentiate the peristaltic

waves of the proximal and distal colons. Furthermore, the transverse colon and descending colon do not have taenia and haustra, ending in the rectum (Smith, 2014).

The proximal colon has small protrusions in the mucous layer, called warts, that increase the absorption area of this region, in addition to having a function in the mechanical separation of intestinal contents. The *defusus colli* region is extremely vascularized and has many innervations, while the *fusus colli* is abundant in goblet cells (large mucus secretors). The region of the distal colon has a thin-walled part with smooth mucosa and crypts covered by goblet cells; it is in this region where hard fecal pellets are found (Smith, 2014); and the rest, together with the rectum, have a tubular shape with thicker walls (Davies & Davies, 2003).

Fonty (1979) studied the microbiota of rabbits, from birth to adulthood, assessing the microbial composition of their stomach, small intestine, caecum and colon. In the colon, after 21 days of life, there was a decrease in aerobic bacteria and a gradual increase in facultative anaerobic and strict anaerobic sporulated bacteria, the same happening in the caecum and small intestine. Facultative anaerobic bacteria were composed exclusively of enterobacteria and *Streptococcus*, and only strict bacteria of the *Clostridium* genus were found. Figure 4 displays the types of bacteria found in each of the four organs, from birth to 56 days of age.

Cecotroph formation

Also known as soft feces, cecotrophs are food for rabbits, rich in nutrients not digested by the GIT, and can be reutilized by the animals.

Covered by a layer of mucus, they are easily distinguished from fecal pellets, as they are soft, moist and tend to stick together like bunches, not forming dry spheres. This layer of mucus has the function of protecting the nutrients present in the cecotrophs from acids originating from the stomach, being ingested whole directly from the rectum, so chewing movements do not occur (Vennen & Mitchell, 2009), being a neurological response of licking, with food intake ceasing at this point for the process to occur (Davies & Davies, 2003).

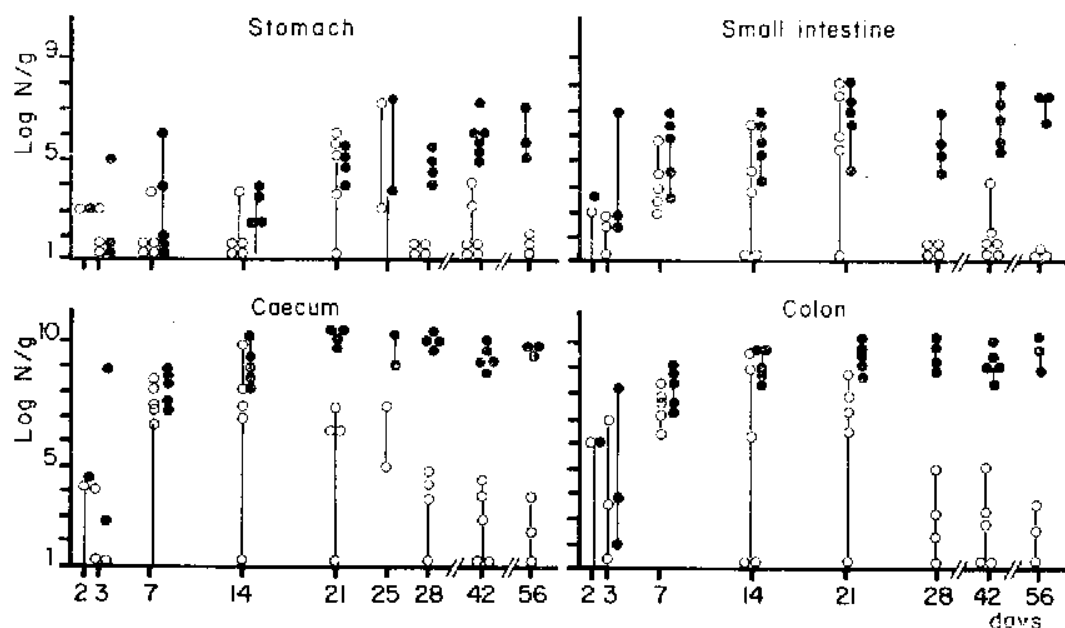


Figure 4. Changes in number of aerobic (○) and anaerobic (●) bacteria in the stomach, small intestine, caecum and colon (Fonty, 1979).

Furthermore, rabbits have a circadian rhythm for the ingestion of cecotrophs; farmed animals ingest predominantly during the light period, while the ingestion of solid food and normal feces production occurs more frequently at night, which differs for animals that live in nature (Blas & Wiseman, 2020).

After the digesta passes through the small intestine, it goes to the *ampulla coli*, which separates large and small particles. These small particles are directed to the caecum, which has many microorganisms, functioning as an anaerobic fermentation chamber. Thus, undigested food arrives, as well as some substances produced by the GIT for the digestion process, along with nutrients that were not absorbed in the anterior intestine, including carbohydrates such as oligosaccharides, cellulose, hemicellulose and pectin, and vegetable proteins embedded in the cell wall.

In this way, the fermentation of nutrients occurs through microorganisms (already mentioned above), with some of these being absorbed by the wall of the caecum for later use (Smith, 2014). However, the colon also plays an important role in the fermentation process of undigested and absorbed nutrients; through antiperistaltic movements and retrograde flow, fine particles and water-soluble substances are sent from the colon to the caecum to be fermented, absorbed and reutilized in cecotrophs (Johnson-Delaney, 2006; Blas & Wiseman, 2020).

From the product of this fermentation, what is not absorbed by the caecum forms a dark and soft paste that is rich in bacteria, amino acids, vitamins (mainly B12 and K), minerals and VFAs and is quickly expelled into the colon through monophasic peristaltic contractions of the caecum, with no separation of liquids and solids from the contents; the *fusus colli* divides the pellets through slower and gentler contractions so that the fluids are not expelled, which does not occur for production of fecal pellets, as there is an increase in contractions in this region so that all fluids are removed, and feces are formed (Davies & Davies, 2003; Smith, 2014).

The colon also has an essential role in the formation of cecotrophs, as it is through the *fusus coli* (proximal colon region) that the interaction of hormones (prostaglandin and aldosterone) that differentiate hard feces from cecotrophs occurs, functioning as a pacemaker to reduce contractions in the proximal colon and increase contractions in the distal colon. After reaching the lumen of the distal colon, lysozyme is secreted and is then incorporated into the cecotrophs (Smith, 2014), which aids in the digestion of microbial proteins (Davies & Davies, 2003). However, the *fusus colli* also plays a role in the secretion of mucus by goblet cells, which accelerates the passage of cecotrophs to the distal colon, in addition to inhibiting the diffusion of electrolytes from the digesta. After they reach the rabbit's anus, the mechanoreceptors in the region are stimulated, and their specific odor is perceived; this way, through various metabolites and hormones, they are then ingested (Smith, 2014).

After ingestion, cecotrophs remain in the stomach for approximately three to six hours (Blas & Wiseman, 2020), which is long enough for the mucus layer surrounding them to be degraded by stomach acids. However, it is in this region that the microorganisms present in the cecotrophs continue to degrade the nutrients present there until the entire mucus layer is disintegrated; when they leave the stomach and reach the small intestine, the normal patterns of digestion and absorption of the nutrients from this content take place (Davies & Davies, 2003; Smith, 2014).

There is an important point to be highlighted about cecotrophy as to its nutritional implications for rabbits, since it is different from coprophagia, which is characterized by consumption of feces from the animal itself or others – quite evident in dogs as an abnormal behavior of the species (Azevedo, Cipreste, & Young, 2007). Cecotrophy represents a digestive strategy for rabbits, not being necessarily a response to nutritional imbalance (Blas & Wiseman, 2020), but a normal habit within their behavioral repertoire. However, there are several factors that affect the production and consumption of cecotrophs, such as age, quantity of food consumed, quality of nutrients present in the food, and physiological state (Davies & Davies, 2003).

The age of the animals influences the proper processing and formation of cecotrophs, as well as their ingestion, as cecotrophy begins between the third and fourth week of the offspring's life, a time when the animals consume almost exclusively a solid diet, and their GIT is already formed (adult pattern). However, it is only after weaning that consumption increases linearly, with production peaking between 63 and 77 days of age, which is compatible with the maximum period required for the growth phase (Blas & Wiseman, 2020). The amount of fiber and protein can also increase or decrease consumption of cecotrophs, as a diet with a higher fiber content stimulates the intake of cecotrophs, while one with a greater amount of protein decreases it (Smith, 2014).

Further considerations

The period until weaning is the most critical in cuniculture, when the highest mortality rate occurs in the litter, since the animals are more susceptible, as they do not have a fully developed immune system or gastrointestinal system. There are challenges to be overcome during this period, mainly to reduce mortality rates, which in Brazil are still undergoing constant evolution and improvements. Therefore, understanding the anatomy and physiology of kits proves to be of great value in reducing these rates, so that management becomes more practical, efficient and adequate, providing producers with different problem-solving alternatives, in addition to greater profit.

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