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# Prenatal and Postnatal Development of the Stomach in Wistar Albino Rats

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**Abstract**
**Aim:** In this study, histological changes in stomach during prenatal and postnatal development were examined.
**Material and Methods:** In this study, 34 female Wistar Albino rats weighing 200-250 g, obtained from Inonu University Experimental Animal Research Lab were used. Stomach samples obtained from prenatal 7,10,14,17, 20 days old fetuses and from postnatal 5,10,15,20 days old newly born and young adult rats were prepared by routine tissue proceeding procedure and examined by light microscopy.
**Results:** In prenatal period, the stomachs of 7,10,14 days old rats were surrounded by stratified columnar or pseudostratified columnar epithelium. Mesenchymal connective tissue surrounded the epithelium. A circular oriented muscle layer was formed in mesenchyme in prenatal 17 days old rats. In prenatal 20 days old rats, extension of the lumen, thickening of the wall, appearance of the foveola and gland-like structures were observed. Epithelium was transformed into simple columnar epithelium in various places. Mucous neck cells in the gland epithelium and outermost serosa layer were identified. On postnatal 5th day, parietal and chief cells could be detected in tubular gastric glands. Myenteric plexus was observed between two muscle layers. On postnatal 10th day, mucus layer was observed on the surface. In subsequent periods, histological properties of stomach were changed and gained adult stomach's properties.
**Results:** It was investigated in which prenatal and postnatal periods the histological features of the stomach of an adult rat were acquired. The obtained data of this study will guide the other related studies.
**Key Words:** Development; Stomach; Prenatal; Postnatal.

Wistar Albino Ratlarda Midenin Prenatal ve Postnatal Gelişimi

**Özet**
**Amaç:** Bu çalışmada prenatal ve postnatal gelişim sürecinde midenin geçirdiği histolojik değişiklikler incelenmeye çalışıldı.
**Gereç ve Yöntemler:** Çalışmada İnönü Üniversitesi Deney Hayvanları Araştırma Laboratuarından temin edilen 200-250 g ağırlığında 34 adet dişi Wistar albino rat kullanıldı. Prenatal 7, 10, 14, 17, 20 günlük fetüslerden, postnatal 5, 10, 15, 20 günlük yavru ratlardan ve genç erişkin ratlardan alınan mide örnekleri rutin doku takip işlemleri ile hazırlanıp ışık mikroskobunda incelendi.
**Bulgular:** Prenatal dönemde 7, 10, 14 günlük ratların mideleri çok katlı prizmatik veya yalancı çok katlı prizmatik epitelle döşeliydi. Epiteli mezenşimal bir bağ dokusu kuşatmaktaydı. Prenatal 17 günlük ratlarda mezenşim içinde sirküler seyirli bir kas tabakasının oluştuğu görüldü. Prenatal 20 günlük ratlarda lümenin genişlediği, duvarın kalınlaştığı, foveola ve bez benzeri yapıların ortaya çıktığı gözlendi. Epitel yer yer tek katlı prizmatik epitele dönüştü. Bez epitelinde boyun mukus hücreleri ve kas tabakasının dışında seroza tabakası ayırt edildi. Postnatal 5. günde tübüler mide bezlerinde pariyetal ve esas hücreler tanınabildi. İki kas tabakası arasında myenterik pleksus görüldü. Postnatal 10. günde yüzeyde mukus tabakasına rastlandı. Bundan sonraki dönemlerde de midenin histolojik özelliklerinin değişerek erişkin midesinin özelliklerini kazandığı görüldü.
**Sonuç:** Erişkin rat midesinin histolojik özelliklerinin prenatal ve postnatal hangi dönemlerde kazanıldığı araştırıldı. Elde edilen bulgular bu konuda yapılacak olan çalışmalara yol gösterecektir.
**Anahtar Kelimeler:** Gelişme; Mide; Prenatal; Postnatal.

## INTRODUCTION

The wall of the stomach consists of typical histological layers including tunica mucosa, submucosa, muscularis and serosa (1-4). Tunica mucosa is composed of epithelium, lamina propria and muscularis mucosa (1,2,5). With naked eye, the iner surface of the stomach is indented by the presence of the "rugae," which are produced by the folding of both mucosa and submucosa. The rugae that are absent when the stomach is distended, help to adapt to volume changes. Epithelium, the first layer of the mucosa, covers all over the inner surface of the stomach including the hollows called as 'foveola' or 'gastric pits' (1,3,4,6-8). The downward invaginations of the foveola epithelium into the connective tissue result in the formation of gastric glands. Gastric pits and glands cover over 800m$^2$ surface area (1).

Stomach epithelium, simple columnar epithelium, is both lining and secretory epithelium (1,3,4,6,8). It both provides a protective epithelial surface and also produces mucus against the destructive effects of the acidic content in the lumen. The cells of the surface epithelium are also called as "surface mucus cells" in order to recognize them as a different cell type from the mucus secreting cells of the glands (3,4,8). Oval-shaped nuclei of the surface mucous cells are located at the basal cytoplasm. An extensive granular endoplasmic reticulum around the nucleus and well-developed supra-nuclear Golgi apparatus are observed. Apical cytoplasm is occupied by numerous mucinogen granules. Because mucin does not stain with hematoxylin and eosin method, apical cytoplasm is pale (3,4). However, using special staining methods particularly for glycoproteins mucin accumulated in apical cytoplasm of cells and on the surface of the epithelium is clearly seen. Mucin, with its high bicarbonate content is protective against the harmful effects of acidic chymus (3,4,8). The second layer of the mucosa, lamina propria, is loose connective tissue (1,3-5,6,8). This layer contains sparsely arranged fibers and various connective tissue cells such as fibroblasts, mastocytes, lymphocytes, plasma cells, macrophages and eosinophils (4,6,8). Diffuse and nodular lymphoid tissues can be located in this layer (3). Follicular lymphoid tissue is especially seen in the pylorus (6). Lamina propria is almost entirely occupied by gastric glands (1,3) which are branched tubular glands in type. Glandular epithelium covers the inner side of the glands (3,4,8).

Stomach contains three types of gastric glands that have regional differences. Among these, cardiac glands are the shortest and the rarest glands. They cover less than 10% of gastric mucosa. On the other hand, the glands of the corpus and fundus are the most common glands. In fact, these glands are the main gastric glands. They constitute about 25% of the mucosa (1). Glands in the fundus usually end by dividing into two branches (1,3,4,8). Tubular glands of the cardia, however, are generally coiled, sometimes branched (1,3,6). Pyloric glands coil near muscularis mucosa though they normally follow a relatively straight route along the lamina propria (3,6). The lumens of these glands are recognizably wide.

Anatomically glands have three regions: isthmus, neck and base. In these sections, the predominant cell types are different. Isthmus, the shorter part of the gland, opens into the foveola. Cell proliferation rate is very high in this part. Stem cells are located here. The following 2/3 of the gland, "the neck portion," is close to the surface; the remaining 1/3 of the gland close to the base of the gland is known as "the basal portion." The glands secrete about 2 liters of fluid a day (1,3,4,8). There are five types of cells with different properties on the glandular epithelium (1-7). These are chief cells, parietal cells, neck mucous cells, enteroendocrine cells, and undifferentiated stem cells.

In this study, the histological features of rat stomach in prenatal and postnatal periods were investigated. The development of surface epithelium, glands, connective tissue, muscles and nerve plexuses and the change of adult rat stomach were examined. It was also investigated in which prenatal and postnatal periods; the histological features of the stomach of adult rats were acquired.

## MATERIAL AND METHODS

In this study, 34 female Wistar albino rats, each weighing 200-250 g, were used. The rats were obtained from Inonu University Experimental Animal Research Laboratory. During the course of our study, which was approved by the ethics committee (approval no: 2009/24), we have complied with the principles of the "Guide for the Care and Use of Laboratory Animals."

The rats were divided into ten groups, five of which were used to examine the prenatal developmental periods while four groups were designed to examine the postnatal development periods. The last group consisted of young adult rats. In the first nine groups, fetuses or neonates were evaluated.

Experimental groups were established as follows:
1 Group (n = 7): Prenatal 7th day fetuses,
2 Group (n = 7): Prenatal 10th day fetuses,
3 Group (n = 7): Prenatal 14th day fetuses,
4 Group (n = 7): Prenatal 17th day fetuses,
5 Group (n = 7): Prenatal 20th day fetuses,
6 Group (n = 7): Postnatal 5 days newly born rats,
7 Group (n =7): Postnatal 10 days newly born rats,
8 Group (n=7): Postnatal 15 days newly born rats,
9 Group (n =7): Postnatal 20 days newly born rats,
10 Group (n = 7): Young adult rats.

At the beginning of the experiment, the female rats spent 2-3 hours with male rats. Regarded as pregnant following a vaginal plaque check, female rats were kept under observation afterwards. The day following the first day of the vaginal plaque observation was considered as the first day of pregnancy. Then on the designated gestation periods (on the $7^{th}$, $10^{th}$, $14^{th}$, $17^{th}$ and $20^{th}$ days), the fetuses were removed by using ketamine-xylazine anesthesia and put into 10% formaldehyde solutions. To obtain postnatal pups, delivery of the rats was waited. On the designated the postnatal periods (on the $5^{th}$, $10^{th}$, $15^{th}$, and $20^{th}$ days), newly born rats were anaesthetized through ether anesthesia and placed in 10% formaldehyde solutions. In order to identify the organs, 10% formaldehyde was injected into the cavities of the bodies of the newborn rats. Young adult rat stomachs were removed under anesthesia and placed into 10% formaldehyde solution. After 2-days fixation period, all samples were dehydrated and embedded in paraffin. Series of 4μm thick sections from paraffin blocks were obtained. Sections were stained with Mayer's Hematoxylin-Eosin, Masson's trichrome and Periodic Acid Schiff (PAS) staining techniques (9.10) and then examined and photographed under a Leica DM LB2 light microscope.

## RESULTS

**Prenatal $7^{th}$ day:** At this period, stomach was seen as an oval-shaped organ located in the mesenchymal connective tissue next to the liver. In cross sections, since its general histological characteristics were close to those of the trachea and intestines, its anatomic location and diameter were regarded important to identify it as stomach. The inner surface of the stomach was lined by stratified or pseudostratified columnar epithelium surrounded by a dense mesenchymal connective tissue rich in cells. Many mitotic figures were observed within epithelium. Additionally, a distinctive basement membrane between the epithelium and connective tissue was observed. However, it was not possible to distinguish other histological layers (Fig. 1a).

**Prenatal 10th day:** At this period, stomach lumen was expanded and the wall was thickened. Surface epithelium was still stratified or pseudo stratified columnar epithelium in type. A cellular, dense mesenchymal connective tissue surrounded the epithelium. Many mitotic figures were observed within epithelium and connective tissue (Fig. 1b).

**Prenatal 14th day:** At this period, stomach lumen was more expanded and the wall was more thickened. The epithelium kept its characteristics as stratified or pseudo stratified columnar. There were many mitotic figures in the epithelium and the connective tissue. Epithelium was surrounded by connective tissue rich in cells and capillaries. The basement membranes were clearly observed. Outermost layer, serosa, appeared as a thin squamous epithelium (Fig. 1c).

**Prenatal 17th day:** At this period, the characteristics of gastric epithelium and the underlying connective tissue were unchanged. However, for the first time, a thin continuous circular muscle layer was observed just outside of the connective tissue (Fig. 1d). There were random mitotic figures in the epithelium, connective tissue and muscle tissue. The muscle cell fibers were surrounded by a connective tissue rich in cells. The outermost layer was the serosa (Fig. 1d).

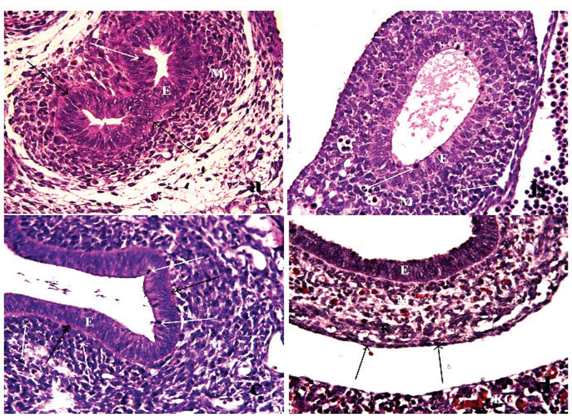

**Figure 1 (a).** Epithelium (E), mesenchymal connective tissue (M), mitotic figures in the epithelium (white arrow) and basement membrane (black arrows) are shown in the figure. PAS; × 40. **(b).** E: Epithelium; M: Mesenchymal connective tissue; Arrows: Mitotic figures. H-E; × 40. **(c).** Epithelium (E), mesenchymal connective tissue (M), mitotic figures in the epithelium and connective tissue (white arrows), basal membrane in the epithelial and connective tissue (black arrows) are seen. PAS; × 40. **(d).** Epithelium (E), mesenchymal connective tissue (M), the muscle layer (K), and liver (KC) can be seen. Masson trichrome; × 40.

**Prenatal 20th day:** At this period, the stomach lumen was considerably enlarged while the stomach wall was likewise thickened. Gastric gave recesses towards the connective tissue that resembled the foveola (Figs. 2a, 2b). These invaginations extending deep into the connective tissue formed gland-like structures composed of epithelial cells around a lumen. The epithelium showed characteristics of both simple and stratified columnar epithelium (Fig. 2a). In the cytoplasm of epithelial cells as well as on the surface of the epithelium a thin layer of PAS positive stained mucus was observed (Fig. 2b). Evidently in the cardia vacuoles in the cytoplasm of the epithelial cells were observed (Fig. 2b).Lamina propria-and submucosa were intermingled due to the lack of lamina muscularis mucosa between them. However, a circular muscle layer could be distinguished encircling the connective tissue from the outside. The place where the outer muscle fibers should have been was more of a connective tissue (Fig. 2a). Mitotic figures were observed in the surface and glandular epithelium, connective tissues and the muscle tissue. Serosa could be also distinguished.

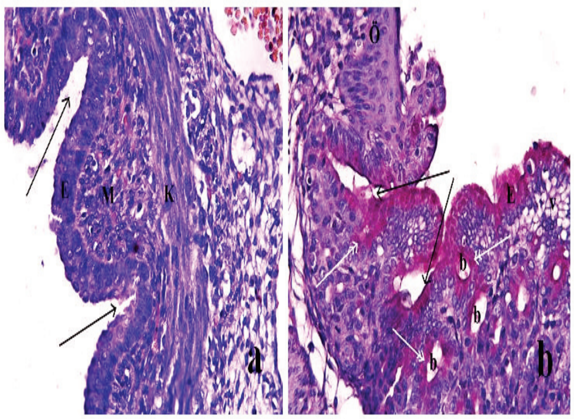


**Figure 2 (a).** Epithelium (E), mesenchymal connective tissue (M), the muscle layer (K), foveola-like structures (arrows) are seen. HE; × 40. (b). Above the esophagus (Ö), epithelium (E), mesenchymal connective tissue (M), gland-like structures **(b).** Foveola-like structures (black arrows) and PAS + mucus on the surface of epithelial cells and glandular epithelial cells can be observed. PAS; × 40.

**Postnatal 5th day:** At this period, epithelium, lamina propria, muscularis mucosa, submucosa, and serosa were visible. Under the single layered columnar epithelium, the lamina propria was occupied by tubular gastric glands. Numerous vacuoles in the cytoplasm of epithelial cells were observed as well. With the PAS staining technique, the surface of the epithelium and the apical cytoplasm of epithelial cells positively stained. Pyramidal-shaped, slightly acidophilic cells thought to be parietal cells along with pale cells thought to be chief cells in the glandular epithelium were detected (Fig. 3). Considerable amounts of mitotic figures were observed in the glandular epithelium. A thin muscularis mucosa composed of circular smooth muscle fibers observed under the lamina propria. Submucosa was loose connective tissues containing blood vessels (Fig. 3). Between the two muscle layers of the tunica muscularis the myenteric plexus was observed. The outermost layer was serosa. Blood vessels and nerves were located in tunica serosa.

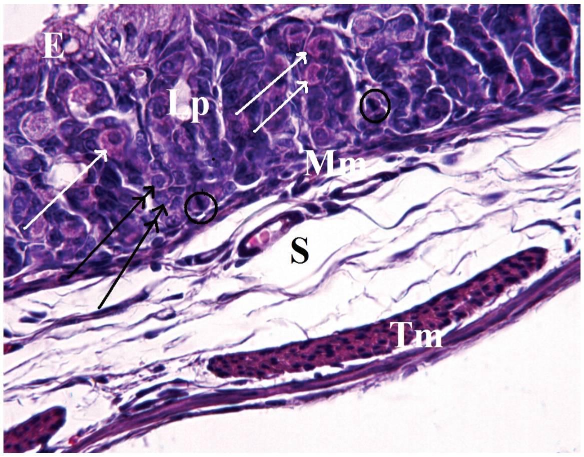


Figure 3.Epithelium (E), lamina propria (Lp), muscularis mucosa (Mm), submucosa (S), tunica muscularis (Tm), parietal cells (white arrows), chief cells (black cells) and mitotic figures (in circles) can be noticed. H-E; × 40.

**Postnatal 10th day:** At this period, all of the layers of the stomach were identifiable. It has been marked that the on the cardia, layers of the esophagus abruptly turned into the layers of stomach. The epithelium of the esophagus that was quite thick was replaced by the epithelium of the stomach. The surface epithelium was simple columnar in type. Foveolas here were sparse (Fig. 4a). There were still some supranuclear vacuoles in the epithelial cells (Fig. 4b). PAS method enabled to see positively stained mucus on the surface, in the apical cytoplasm of both epithelial cells of surface and glandular epithelium of the neck portion of the glands. Lamina propria was occupied by the tubular gastric glands (Figs. 4a, 4b). A prominent dilatation of the glandular lumen was observed especially on the cardia. The parietal and chief cells in the glandular epithelium were easily identified (Fig. 4b). Frequent mitotic figures on the surface epithelium and glandular epithelium were observed. Muscularis mucosa was continuous. Submucosa was loose connective tissue. It was also noteworthy to see collagen fibers concentrating on muscularis mucosa border. Myenteric plexus was detected between the two layers of tunica muscularis. The outermost layer was the serosa (Fig. 4a).

**Postnatal 15th day:** At this period, all layers of the stomach wall could be observed. A sudden change in the stratified epithelium of esophagus was observed on the esohageal-gastric junction where it turned into the simple columnar epithelium of the stomach (Fig. 5a). The epithelium slightly invaginated into the lamina propria, formed shallow foveolas. In the apical cytoplasm of epithelial cells and on the surface PAS-positive mucus was observed. Lamina propria was occupied by the gastric glands (Fig. 5b). Especially in the cardia, lymphoid tissues were observed in this layer. Muscularis mucosa was now a very thick layer (Figs. 5a, 5b). Submucosa carried the characteristics of loose connective tissues containing many blood vessels. Tunica muscularis consisted of two muscle layers. Between these two layers, myenteric plexus was frequently detected. Serosa was more of a loose connective tissue (Fig. 5a).

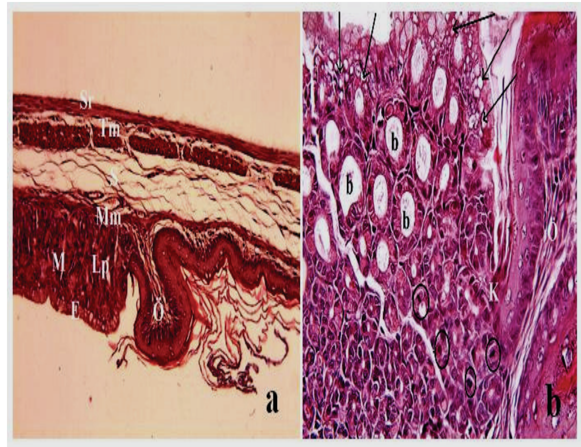


**Figure 4. (a).** Esophagus (Ö), stomach (M), epithelium (E), lamina propria (Lp), muscularis mucosa (Mm), submucosa (S), tunica muscularis (Tm), serosa (Sr) can be seen in this image. HE; × 20. **(b).** cardia glands (b), vacuolisation (V), mitotic figures (in circles) can also be seen. H-E; × 40.

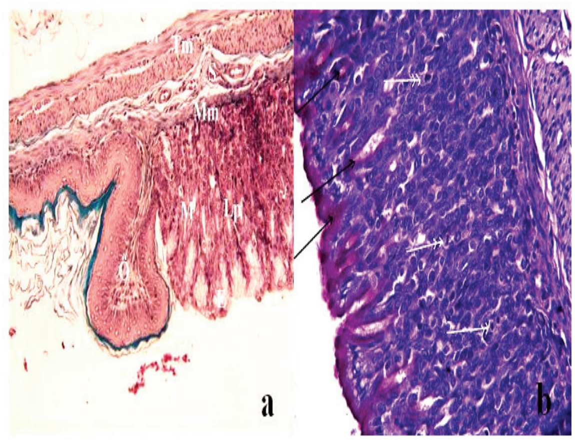


**Figure 5 (a).** Esophagus (Ö), stomach (M), epithelium (E), lamina propria (Lp), muscularis mucosa (Mm), submucosa (S), tunica muscularis (Tm), serosa (S) are shown in the figure. Masson Trichrome; × 20 **(b).** PAS + staining on the surface epithelium and glandular epithelium (arrows) and mitotic figures (white arrows) can be seen. PAS; × 40.

**Postnatal 20th day:** All layers of the stomach wall were visible. The epithelium was simple columnar epithelium (Fig. 6a). Lamina propria was occupied by the tubular glands (Figs. 6a, 6b). In addition to the parietal cells, chief cells were observable, as well. Muscularis mucosa was formed by circular muscle fibers. Submucosa was loose connective tissue (Figs. 6a, 6b). Tunica muscularis composed of two layers. Between these muscle layers was the myenteric plexus. The outer surface was covered by serosa (Fig. 6b).

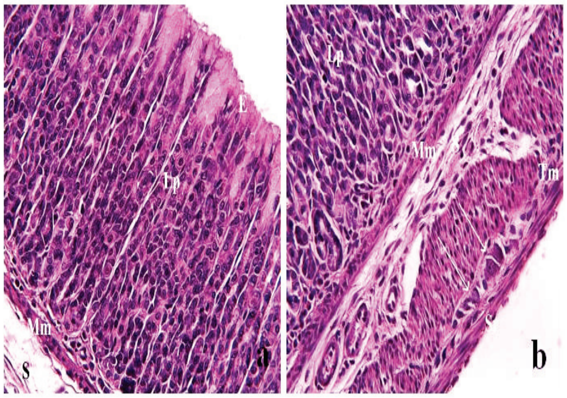


**Figure 6 (a)**. Epithelium (E), lamina propria (Lp), muscularis mucosa (Mm), submucosa (S) can be seen in the figure. HE; × 40. **(b).** Epithelium (E), lamina propria (Lp), muscularis mucosa (Mm), submucosa (S) tunica muscularis (Tm), serosa (Sr), myenteric plexus (arrows) are also presented above. H-E; × 40.

**Young Adult:** All layers of the stomach wall were observed (Fig. 7a). In addition to chief cells and parietal cells in the glandular epithelium, mucous neck cells could also be identified. PAS + staining was observed on the surface epithelium and glandular epithelium. At this period, the mucus layer covering the surface of the epithelium was significantly thickened (Fig. 7b).

Muscularis mucosa consisted of circular muscle fibers. Submucosa was loose connective tissue containing blood vessels and fat cells. Tunica muscularis consisted of two muscle layers. Inner muscle layer was quite thick. Between the two layers, myenteric plexus was observed. The outer surface was covered with serosa (Figure 7a).

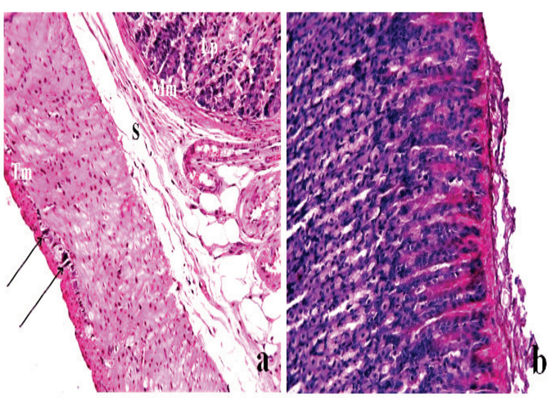


**Figure 7 (a)**. Lamina propria (Lp), muscularis mucosa (Mm), submucosa (S), tunica muscularis (Tm), myenteric plexus (arrows) are seen in the figure. H-E; × 20. **(b).** Mucus is visible on the surface, on the surface of epithelial cells and in the gland lumen. PAS; × 20.

## DISCUSSION

In mammals, stomach develops with the expansion of primitive intestinal tract distal of esophagus. Compared to other parts of the intestinal tract, stomach is wider in diameter which makes it the first organ to be detected (11, 12). As a result of faster growth of dorsal wall compared to the ventral wall, greater curvature and small curvature develops respectively. With a $90^0$ clockwise rotation, the lesser curvature locates on the right and the greater one on the left. By cephalocaudal rotation, cardiac portion moves to slightly downwards, pyloric part moves to the upward as expected (11,12,13).Some of the typical anatomical features of the stomach such as large and small curvatures, fundus, corpus, and pylorus can be detected in humans in the 14th week (14).

In addition to the changes in location of the stomach, its development brings about some other changes like widening of the lumen, thickening of the wall, histological changes, and cellular differentiation. As the developing fetus absorbs amniotic fluid, the diameter of the stomach widens (14). In our study, we observed that lumen was expanded and wall was thickened during prenatal and postnatal development.

There are some studies reporting that the stomach epithelium acquires a stratified characteristic in rats through $13^{th}$ to $19.5^{th}$ intrauterine days (15-22). Aşar *et al.* observed stratified columnar epithelium on the stomach wall on $17^{th}$. day (15). Gastric epithelium shows the characteristics of stratified or pseudostratified epithelium in $4^{th}$. intrauterine week in humans (23, 24), on $18^{th}$-$19^{th}$ days in rabbits (25.26). We also defined the gastric epithelium as stratified or pseudostratified epithelium on $20^{th}$ intrauterine day in our study. We have also witnessed that the epithelium transformed into a single-layered high columnar epithelium in some sections in $20^{th}$ day. There are conflicting results related with the period of the transformation of the epithelium from stratified to simple columnar in rats. Aşar *et al.* have shown how the gastric epithelial was made up of 1-2 cell layers on $18^{th}$. and $19^{th}$. days (15). There are some other studies reporting such a change on $15^{th}$ (27), $19^{th}$ (28-30), and 20-$21^{th}$ days (20,21,31).

Familar *et al.* have observed that the stomach epithelium was a single layered cuboid epithelium on $18.5^{th}$ day and a simple columnar epithelium on $19.5^{th}$ day. We suggest that the transition into a single layered epithelium occurs after $20^{th}$ day. Indeed, Ashar *et al.* have reported this transformation on $20^{th}$ day (15). In humans, the transformation from stratified epithelium to a single layered epithelium occurs in 11-$17^{th}$ weeks (32,33). The mechanism that enables this transformation, however, is not known. Nonetheless, it is thought that these cells might be migrating away or simply become extinct through necrosis or apoptosis (16).

In our study, we have observed that, in the early stages of development, the border between the epithelium and the mesenchymal connective tissue was straight. Then we found out that this border got slightly indented on intrauterine $20^{th}$ day. Aşar *et al.* have reported that the border becomes irregular on $17^{th}$ day (15). It is known that the interaction between epithelial cells and mesenchymal cells regulates the proliferation and differentiation of the epithelial cells (34). Fukamachi *et al*. have shown that in the absence of mesenchymal cells, the glandular epithelial cells change into surface mucus cells, not into parietal and chief cells (35).

As the rugae and the foveolas are observed, gastric mucosa in humans starts to change towards the end of the 2nd month. The cell differentiation that begins in early fetal period continues until late fetal period (12). It has been reported that the foveola is formed on 19.5th day in rats (17,22). Several results have been reported concerning the period of appearing of the glands. There are studies indicating that glands can be seen on intrauterine 18th (15.16), 19.5th (17) or 21.5th days (22). On intrauerine 20th day, gastric glands deepen and continue to grow (15). In our study, we have observed the epithelium initially invaginates into the connective tissue and creates foveola and gland-like structures on intrauterine 20th day. Indeed, it has been claimed that the recesses on the surface of the epithelium create foveolas on intrauterine 17th day (15). Glands grow rapidly, especially after delivery. In 4th week after birth, glands look like those of adults (22). Similarly, we have also discovered that glands rapidly extend and become similar to those of the adults particularly after birth. It has been suggested that type 1 collagen in the lamina propria plays a role in the folding of the mucosa and the formation of glandular structures (16). On 16th day, type 1 collagen in the stomach was only seen in sections adjacent to the esophagus. On 18 th day, the density of the collagen fibers increases and they begin to be seen in the submucosa and serosa (16). In late embryonic period, on 16-21th days, there are significant structural changes the epithelium of the gastric glands (36,37); however, on 16-18th days, there is not any cell differentiation in rat embryos (28,37). It is suggested that ingested amniotic fluid starting from the intrauterine 18th day (38) may affect gastric epithelial cells to proliferate and differentiate (16). Although some studies reports that differentiation in rats begins from 21st day (29), some others reports that surface mucus and mucus neck cells are distinguishable on intrauterine 19th day (21,28,29,40). Andersson *et al.* have reported that the cells that contain mucin granules have been formed on 19.5th day (17). The secretory granules seen in the apical cytoplasm of the surface of epithelial cells increase between the 20th-21st days (40). Furihat *et al.* (41) have observed the neck mucous cells in the epithelium of the gastric glands in the first 10 days after birth by electron microscopic methods. Likewise, in our study, we have been able to distinctly identify the cells containing PAS positive stained secretory granules on the surface epithelium and primitive glandular epithelium on intrauterine 20th day.

Although it has been reported that chief cells in rats can easily be detected on postnatal 16-17th days by electron microscopy (41), some researcher suggest that chief cells appear on intrauterine 20th day (29). Pepsinogen C-positive cells, although rare, could be marked on 18.5th day. On 20.5th day, however, it has been observed that all of these cells are randomly dispersed on the gland (22). Furihat *et al.* have shown immature chief cells on the gastric glands within the first 10 days after birth by electron microscope (41). It has been claimed that many postnatal secretion granules have decreased during the first ten days after birth and then acquired a similar structure to that of adults on the following 20th-25th days (41). There have been conflicting results that even on intrauterine 16th day and on postnatal 14th day there is not any chief cells in rats (42). In our study, we identified chief cells on postnatal 5th day by light microscope. Conflicting results have also been reported about the appearance of the parietal cells in rats. This period is between intrauterine 19th-21th days (15,18,19,21,22,27,28,40). Parietal cell marker H, K-ATPases have been detected on 16th-18th days for the first time (16). We observed the parietal cells at a later stage, on the 5th day after birth. It could be possible to identify parietal cells with electron microscopic and immunohistochemical methods at an earlier stage. It is known that HCl acid secretion from parietal cells in humans starts right before birth (12).

In the present study, connective tissue, rich in cells and vessels but poor in fibers surrounding the epithelium kept growing its thickness during the prenatal period. Because muscularis mucosa was detectible on postnatal 5th. day, it was impossible to distinguish the lamina propria from submucosa. However, Tommeras *et al.* have identified the layers of lamina propria and submucosa on 18th. of pregnancy (16). Although the thickness of the submucosa during the development stages in our study increased, this layer was of loose connective tissues even in young adults. Within this layer, we have not defined any submucosal nerve plexus in any of the periods. There is just one study reporting that the submucosal plexus in rats appears on 18th. day (15). In our study, we identified the first muscle layer of the stomach wall on intrauterine 17th day. This was a continuous circular muscle layer extending around the connective tissue. We observed tunica muscularis for the first time on postnatal 5th. day. Aşar *et al.* observed the circular muscle on intrauterine 18th. day, and the entire muscle layer on 21st day (15). Tommeras *et al.* have similarly reported that the muscle layers appear on 18th day (16). It has been stated that the neuroblasts began to accumulate to form the myenteric plexus on 18th day while the entire myenteric plexus appears on 21st day (15). Seki *et al.* have claimed that the myenteric plexus appears on 18th day (40). We were not able to observe myenteric plexus in the prenatal period in our study though we observed an intensive plexus extending between the muscle layers on postnatal 5th. day. Serosa, with its specific features, has been defined on intrauterine 18th day (16). Bayram *et al*. have reported that this layer was composed of a single layered cubical epithelium on 15th day (43). We observed that the outer surface was surrounded by a single layered squamous epithelium from 14th day.

Within 1 month of birth, in line with some dietary changes, significant structural and functional changes occur in the mucosa of the digestive system in rats (41,44,45). We observed that layers gradually become similar to those of the adults during prenatal and postnatal periods.

In our study, through an examination of prenatal and postnatal development, anatomical and histological changes of the stomach were identified. By using three different staining methods, various alterations of cells and tissues were studied through their developmental stages. The detailed information obtained from this study might form the basis for future experimental works.

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