

## Comparative endoscopic evaluation of normal and ulcerated gastric mucosae in Thoroughbred foals

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**ABSTRACT.** To contribute to early diagnosis and treatment of gastric ulcer of foals, we examined the gastric mucosa of healthy and affected foals using an endoscope. In healthy foals, the characteristic changes in the development of the squamous mucosa were seen mainly in the squamous mucosa, and maturation of the squamous mucosa in the greater curvature (GC-S) occurred more slowly than that of the squamous mucosa in the lesser curvature (LC-S). Epithelial desquamation in the LC-S and GC-S was observed between 6 and 90 days but was not observed in the LC-S at about 60 days, whereas it was observed in the GC-S until 90 days old. These findings suggest that there is a difference in the development of the gastric mucosa by region and that desquamation continues over a term longer than studies have reported in the past. In the affected foals, the minimum age at which gastric ulcer was observed was 4 days old. Gastric ulcers formed predominantly in the squamous mucosa (LC-S and GC-S) of foals with an immature mucosa before the weaning period, and the peak incidence occurred between 61 and 90 days old. The differences in the ulceration sites were considered to depend on the difference in the development (maturation) stage of the squamous mucosa. The grading score of the gastric ulcer increased with the growth of the affected foals. The gastric ulcer might be enhanced greatly by stress in the weaning period.

**KEY WORDS:** endoscopy, equine gastric ulcer, foal

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Veterinary clinical reports state that gastric ulcer occurs frequently in 25 to 50% of foals in Western countries [1, 9, 10, 16, 18]. This disease often heals naturally without specific clinical signs [14]. When associated with severe digestive or respiratory disease, it may have an adverse effect on growth of the foal. The disease may lead to gastric ulcer perforation, and it can lead to death in the worst cases [1, 12]. Occurrence of gastric ulcers in foals in the Hidaka region of Hokkaido, Japan, which is the main racehorse producing area, has also been observed. Death caused by gastric ulcer perforation, mainly in the squamous mucosa, adjacent to the margo plicatus in the lesser (LC-S) and greater curvature (GC-S), has been found to occur in 7 to 16% of the foals suffering from various diseases during the year after birth [21, 22]. Control of feeding and hygienic management of newborn horses is an important factor in the production of racehorses. Therefore, identification of the factors for prevention of gastric ulcers in foals is very important. It has been reported that foals suffering from a gastric ulcer often experience concomitant diarrhea and poor appetite, which are the most

frequent clinical signs. In addition, poor growth, rough hair coat, potbellied appearance, bruxism, dorsal recumbency, excessive salivation, interrupted sucking and colic have been described [1, 9, 18]. A few clinical pharmacological treatments for gastric ulcer have been reported [1, 2, 14], but several problems concerning pathogenic factors have not been solved. We performed endoscopic evaluations to clarify the endoscopic appearance of gastric ulcers of 56 newborn horses in the Hidaka region, including comparison with the normal gastric mucosae of 12 healthy horses. The purpose of this study was to describe the gastric mucosal changes by location in healthy newborn foals from 6 to 60 days of age and the characteristics of gastric mucosal changes of foals having gastric ulceration throughout the first several months of their lives.

### MATERIALS AND METHODS

*Healthy horses:* Eleven foals (7 males and 4 females under one year old) and an yearling female Thoroughbred were used for evaluation of the development stages of the gastric mucosae of healthy horses. Details of the program for endoscopic examination are summarized in Table 1.

*Affected foals:* In the clinical field, it has been empirically demonstrated that foals suffering from gastric ulcer frequently exhibit depression, dysorexia or diarrhea [1, 3, 11]. Fifty-six foals having these symptoms were used for examination of gastric ulcer by endoscope, as shown in Table 2. We devised a grading system for the gastric ulcers

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Table 1. Endoscopic examination of the healthy horses

Examined horse	Sex	Age(days) at the time of the examination														Number of examinations			
		1-10 5	11-20 15	21-30 25	31-40 35	41-50 45	51-60 55	61-70 65	71-80 75	81-90 85	91-100 95	101-110 105	111-120 115	121-130 125	460	480			
1	M	•			•													2	
2	F		•															1	
3	F			•														1	
4	F				•													1	
5	M					•												1	
Foal 6	M								•									1	
7	M									•								4	
8	F										•						•	4	
9	M																•	4	
10	M																•	4	
11	M																•	4	
Yearling	F																•	•	2
Total	(12)																	29	

M: male, F: female. The number of horses is shown in parentheses, Eleven foals (7 males and 4 females under one year old) and an yearling female Thoroughbred were used for evaluation of the development stage of the gastric mucosa of healthy horses.

Table 2. Endoscopic examination of the affected horses

Age (days)	Number of examinations at each age (days)		
	Male	Female	Total
4-30	5	3	8
31-60	9	8	17
61-90	10	9	19
91-120	7	1	8
121-198	2	2	4
Total	33	23	56

of the foals according to Andrews' criteria [3] and calculated the distribution of the lesions. The grading system was as follows: A score of 1 indicates that the mucosa is intact, but associated with areas of hyperemia with erosion (Fig. 1A). A score of 2 indicates a small, single or multifocal superficial ulcer with hyperemia (Fig. 1B). A score of 3 indicates a large, single, multifocal or extensive superficial ulcer with hyperemia (Fig. 1C). Finally, a score of 4 indicates extensive lesions with areas of apparent deep ulceration (Fig. 1D).

**Endoscopic examination:** The endoscope (VQ-8303A, Olympus, Tokyo, Japan) used in the present study has an effective length of 3,000 mm, a tip diameter of 10.6 mm, a suction unit and an image recording apparatus. The endoscopic procedure was performed according to previous reports [10, 13]. For the purpose of sedation and pain relief, a combined solution of xylazine (0.5 mg/kg, IV, Nippon Zenyaku Kogyo Co., Ltd., Koriyama, Japan) and butorphanol (0.01 to 0.02 mg/kg, IV, Bristol-Myers Squibb Co., Tokyo, Japan) was used before endoscopic examination. The endoscope was inserted via the nasal cavity of foals and reached the stomach cavity expanded by air from a biopsy channel. Endoscopic examination was performed on 4 regions of the squamous mucosa in the lesser curvature (LC-S), squamous mucosa in the greater curvature (GC-S), glandular mucosa in the greater curvature (GC-G) and pylorus (P).

Statistical analysis of the mean scores was performed with the *t*-test.

## RESULTS

**Healthy horses:** At the 6th day after birth, the margo plicatus was clear, and serrated ridges were not noticeable. The squamous mucosa (LC-S and GC-S) wall was very thin, and part of the spleen attached to the outer wall of the stomach was observed through the thin gastric mucosa. The spleen was observed at around the 30th day. The GC-G exhibited a thin membrane-like appearance with a clear color. The margo plicatus became clear at 14 days old, and the formation of serrated ridges was not observed at that time. The squamous mucosa wall thickened somewhat, had a translucent luster and appeared to be wet. The GC-G was wet and pink in color. At 21 days old, the margo plicatus showed a serrated ridge. The squamous mucosa wall thickened further, and the clarity of the stomach wall was lost. The GC-G was wet and had a surface structure containing irregularities that were finely granular. At 28 days old, a serrated ridge was evident at the boundary of the squamous mucosa and glandular part. The blood vessels running through the thickened stomach wall were clearly observed. The GC-G also thickened, and the granular structure of the mucosal surface showed a more pronounced pink color. Throughout the period from 6 to 28 days old, epithelial desquamation was observed characteristically on the entire surface of the squamous mucosa. Although epithelial desquamation of the LC-S was noted until 60 days old, it was still observed in the GC-S at 90 days old (Fig. 1). At around 120 days old, the squamous mucosa wall had an increased thickness, and the serrated ridges had grown, appearing similar to those observed in the squamous mucosa of a yearling horse. After 30 days, the GM thickened and showed a reddish color. The granular structure of the mucosal surface was more marked. The thickened squamous mucosa wall of the yearling lacked epithelial desquamation,

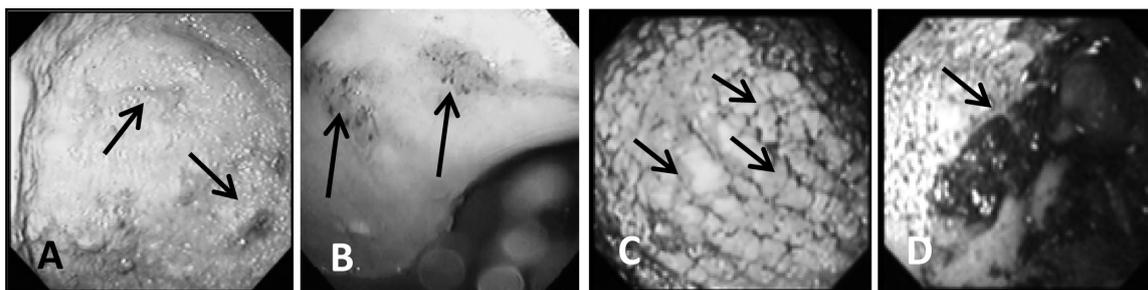


Fig. 1. A grading system for the gastric ulcers of foals (modified Andrews' criteria, 1999). (A) Score 1: the mucosa is intact, but associated with areas of hyperemia with erosion (arrows). (B) Score 2: small, single or multifocal superficial ulcers with hyperemia (arrows). (C) Score 3: large, single multifocal or extensive superficial ulcers with hyperemia (arrows). (D) Score 4: extensive lesions with areas of apparent deep ulceration (arrow).

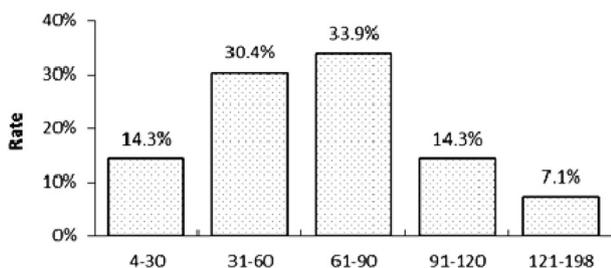


Fig. 2. Incidence of gastric ulcer at each age (day). The incidence (30.4%) of gastric ulcer sharply increases between 31 and 60 days old. The highest incidence (33.9%) of gastric ulcer is between 61 and 90 days old. The incidence (14.3%) of gastric ulcer sharply declines at 91 days old or older.

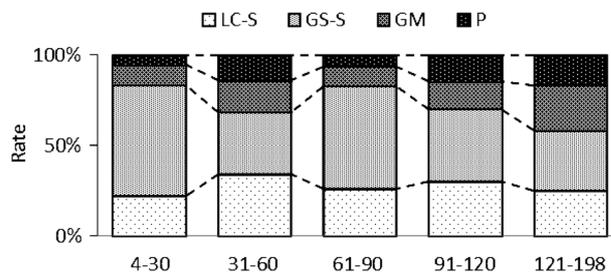


Fig. 3. Distribution of ulcers in each gastric mucosa in the 56 affected foals. Gastric ulcers occurred more frequently in the squamous mucosa (LC-S and GC-S) (74.8%) than in the glandular mucosa (GC-G and P) (25.2%) during the period of examination.

and the surface of the mucous membrane showed dryness. The mucosa of the gastric fundus and pylorus exhibited a shiny and smoothly granular structure. During the period of endoscopic examination, there were no abnormalities in the gastric mucosa in any of the foals.

**Affected foals:** The number of foals having a gastric ulcer during the 198 days after birth is summarized for each 30-day period in Fig. 2. The minimum age of the foals having a gastric ulcer was 4 days old. The incidence of gastric ulcer sharply increased by 30.4% after 31 days old. The highest incidence (33.9%) of gastric ulcer was found between 61 and 90 days old. After 91 days old, the incidence of gastric ulcer sharply declined (14.3%).

The age (days old) at the time of endoscopic examination and distribution of gastric ulcers in 56 foals are shown in Fig. 3. Gastric ulcer occurred more frequently in the squamous mucosa (LC-S and GC-S) (74.8%) than the glandular mucosa (GC-G and P) (25.2%) during the period of examination. In the group of foal at up to 30 days old, gastric ulcer was frequently observed in the GC-S. In the group of foal at 31 to 60 days old, the ulcers increased in the LC-S in a manner similar to that in the GC-S. In the group of foals at 61 to 90 days old, the incidence of gastric ulcer sharply increased by more in the GC-S than in the LC-S. Gastric ulcers formed predominantly in the GC-S between 4 and 90 days old and had a peak incidence between 61 and 90 days

old. In the group of foals at 91 to 120 days old, the incidence of ulcers was reduced, and they were found predominantly in the squamous mucosa (LC-S and GC-S). At over 120 days, there were no differences observed in the incidence of ulcer in the 4 parts of the gastric mucosa.

The age (days old) at the time of endoscopic examination, and the grading scores of gastric ulcers in 56 foals are shown in Fig. 4. The average score for gastric ulcers in each of the parts showed a tendency to increase over time. In the group of foals at up to 30 days old, the mean  $\pm$  SD grading score for ulcers at each mucosal site was  $0.53 \pm 0.24$  (LC-S,  $0.13 \pm 0.13$ ; GC-S,  $0.75 \pm 0.16$ ; GC-G,  $0.88 \pm 0.40$ ; P,  $0.38 \pm 0.26$ ). In the group of foals at 31 to 60 days old, the mean  $\pm$  SD grading score for each mucosal site was  $0.53 \pm 0.21$  (LC-S,  $0.24 \pm 0.14$ ; GC-S,  $0.71 \pm 0.22$ ; GC-G,  $0.69 \pm 0.27$ ; P,  $0.50 \pm 0.20$ ). In the group of foals at 61 to 120 days old, the mean  $\pm$  SD grading score in the GC-S was between  $1.26 \pm 0.25$  and  $1.13 \pm 0.55$ . The mean  $\pm$  SD grading score in the GC-G was between  $2.00 \pm 0.38$  and  $1.50 \pm 0.60$ . In the group of foals at more than 120 days old, the mean  $\pm$  SD grading score in each mucosa was  $1.19 \pm 0.68$ .

DISCUSSION

**Healthy horses:** A few reports have described the development process of the gastric mucosa of neonatal foals using

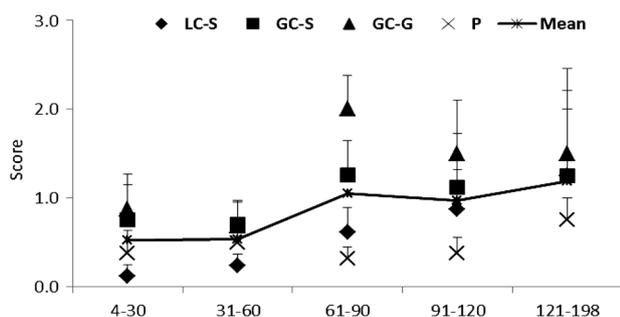


Fig. 4. The average score of gastric ulcers in all parts of the gastric mucosa. In the group of foals at up to 30 days old, the mean  $\pm$  SD grading score of ulcers for each mucosal site was  $0.53 \pm 0.24$  (LC-S,  $0.13 \pm 0.13$ ; GC-S,  $0.75 \pm 0.16$ ; GC-G,  $0.88 \pm 0.40$ ; P,  $0.38 \pm 0.26$ ). In the group of foals at 31 to 60 days old, the mean  $\pm$  SD grading score for each mucosal site was  $0.53 \pm 0.21$  (LC-S,  $0.24 \pm 0.14$ ; GC-S,  $0.71 \pm 0.22$ ; GC-G,  $0.69 \pm 0.27$ ; P,  $0.50 \pm 0.20$ ). In the group of foals at 61 to 120 days old, the mean  $\pm$  SD grading score in the GC-S was between  $1.26 \pm 0.25$  and  $1.13 \pm 0.55$ . The mean  $\pm$  SD grading score in the GC-G was between  $2.00 \pm 0.38$  and  $1.50 \pm 0.60$ . In the group of foals at more than 120 days old, the mean  $\pm$  SD grading score for each mucosa was  $1.19 \pm 0.68$ . The grade of gastric ulcer shows a tendency to increase with age in days.

an endoscope [9–11, 13–15]. However, long and continuous observations of the mucosal development of the stomach for 119 days after birth have not been reported as far as we know. In this report, endoscopic observation revealed the development process of the gastric mucosa of the foal, during the 4 months following birth. Immediately after birth, part of the spleen attached to the outside stomach wall and was observed through the thin gastric mucosa. The serrated ridge (margo plicatus) was confirmed after the 21st day. After 28 days of development, the stomach wall was thick enough to prevent observation of the spleen through the wall. The appearance of the mucosal surface was very similar to that of a yearling horse. During examination, formation of epithelial desquamation on the mucosal surface was characteristically observed in the squamous mucosa (LC-S and GC-S). Histologically, the stratum corneum of the squamous mucosa forms beginning in the late fetal stage, and the stratum corneum grows slowly thicker after birth [15]. The keratinized epithelium of the stratum corneum detaches from the mucosal surface gradually, and this is called epithelial desquamation. Epithelial desquamation is considered a physiological phenomenon and is characteristic of the development process of the gastric mucosa [11, 15]. In our study, endoscopic examination revealed the physiological development process of the gastric mucosa during the 4 months following birth. Earlier studies reported that epithelial desquamation of the squamous mucosa disappears at around 40 days old [16]. However, epithelial desquamation was observed in the LC-S in our foals until 60 days old and in the GC-S until 90 days old. This finding suggests that there is a difference in the development of the gastric mucosa by region and that desquamation can continue over a long term, a term longer than studies have previously reported.

*Affected foals:* As reported in Western countries, gastric ulcers of foals in Japan (Hidaka district) occur between 30 and 90 days old, but the reason for this is still unclear [3]. A deficiency in passive immunity is considered to be one of the internal factors that contribute to gastric ulcers that occur frequently in this period [7, 8]. Many severe diseases, such as pneumonia (e.g., *Rhodococcus equi*) [19], enteritis (e.g., *Rotavirus*) [5, 6, 22], infectious arthritis and osteomyelitis occur frequently in foals with immunodeficiency [7]. Gastric ulcer is also considered to be associated with severe diseases in foals [11]. On the other hand, changes in feed and rearing environment can be considered as external factors. In the Hidaka district, the weaning of foals usually begins at around 100 days old and ends at around 180 days [4]. In the healthy foals, the mother's milk and secretion of by the foal prompts the proliferation of epithelial cells and maturation of the gastric mucosa in preparation for weaning [17]. While living with the mother, the growing foal may frequently eat the concentrated feed given to the mare [20]. The decreases in gastric juice pH, intake of the mother's milk and saliva secretion caused by this surreptitious eating are considered to disturb the development of the gastric mucosa before controlled weaning. Our study revealed that maturation of the gastric mucosa of the foal occurs up to at least 90 days old. Before weaning, surreptitious ingestion of the mother's feed may be a major factor inducing gastric ulcers in foals [20]. Therefore, the deficiency of passive immunity and failure of feeding management can be considered important factors in the occurrence of gastric ulcers in foals before weaning. The increased gastric ulcer score along with age in the affected foals suggests that these factors may contribute to formation of severe lesions before weaning of the foals.

On the other hand, ulcers in the weaning period after 120 days old showed a high score in the present study. Weaning of foals may be involved in weakening the immune system and weight loss [8]. These factors may have doubled the load factor for the affected foals.

The gastric ulcers were found to have occurred mostly in the squamous mucosa (LC-S and GC-S) throughout the examination period. The results suggest that gastric ulcers may occur given the specific background of the development process of the mucous membrane and structure of the stomach. The mucosal surface of the GM is protected by mucus produced by the surface mucus cells, and secretion of digestive juice is not active in the lactation period. The membrane of the squamous mucosa (LC-S and GC-S) lacks surface mucus cells and is protected solely by the action of saliva. The mother's milk in the lactation period contributes to protect the mucosal membrane and to the development of the gastric mucosal epithelium [17]. Therefore, anatomical and functional differences of the stomach, which are horse specific, may cause the differences in sites of lesions and scores of gastric ulcers caused by the various internal and external factors. In other words, when the causes of gastric ulcer overlap, the squamous mucosa is the most affected region, and the lesion may occur most frequently in the GC-S, in which development of the mucosa continues until around 90 days old.

The results of the present study are summarized as follows. The process of development of the gastric mucosa of healthy foals during the 119 days from the 6th to the 125th day after birth was revealed in this study. Characteristic changes were seen in the squamous mucosa (LC-S and GC-S), and the maturation of the squamous mucosa (LC-S) was more rapid than that in GC-S. The epithelial desquamation of the squamous mucosa (LC-S and GC-S) indicates the process of development of the squamous mucosa membrane and is considered to be a normal physiological phenomenon. Gastric ulcers formed predominantly in the squamous mucosa (especially in the GC-S) due to the immature mucosa of the foals before the weaning period, and the peak incidence was between 61 and 90 days.

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