Invited Review

Functional morphology of the equine pelvic flexure and its role in disease. A review

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Summary. The hindgut is the major site in the horse for nutrient digestion and absorption. Most of this activity occurs in the large intestinal compartments, i.e., cecum, right and left ventral colon and left and right dorsal colon. The colonic pelvic flexure is a short and narrow loop connecting the left ventral and left dorsal colon. It is not significantly different in digesting and absorptive processes but plays an important functional role in regulating colonic aboral and retropropulsive transit of digesta through its motility pacemaker activity. The pelvic flexure also contributes to the pathophysiology of colic, the leading cause of death in horses. Its narrow lumen may contribute to colonic impaction, and malfunctions of the pacemaker may contribute to volvuli and colonic displacements. Neuronal and ganglion density of the myenteric plexus is increased at the pelvic flexure and adjacent left dorsal colon pacemaker region. Contractile activity, vasoactive intestinal peptide (VIP) and neurokinins-1 and -3 are all enhanced in the pelvic flexure. The mucosa histologically resembles that of the ventral and dorsal colon, with apically-granulated principal cells and goblet cells lining the luminal surface. Clustered intranuclear inclusions resembling the cytoplasmic granules are also observed by electron microscopy in the principal cells as elsewhere in the horse colon. Further neuroendocrine and morphologic investigation of the pelvic flexure is warranted due to the great importance of this localized region for normal function and pathophysiology.

Key words: Horse, Colon, Motility, Pacemaker

Introduction

The horse is a monogastric herbivore with a hindgut highly specialized for fiber, i.e., insoluble carbohydrate, digestion. Similarly to what occurs in ruminants, fiber digestion provides a major source of energy for the horse following production of volatile fatty acids by microbial activity. For maximal efficiency the horse's hindgut has evolved in order to create an environment favorable for microbial development and fiber digestion. Special motility patterns to keep undigested fiber in the main digestive physiology, the activity of the pelvic flexure pacemaker has also been considered an important feature in colic pathophysiology. The relatively narrow lumen of the pelvic flexure and the retropropulsive peristaltic contractions seem to contribute to the formation of impaction. Additionally, large colon displacements and volvuli are thought to result from malfunction of the pelvic flexure pacemaker (Sellers et al., 1982a, b, 1984; Sellers and Lowe, 1986). Despite its recognized importance, many of the morphologic and physiologic aspects of the pelvic flexure remain unknown. The objective of this report is to review the morphologic and physiologic aspects of the equine pelvic flexure in relationship to the large colon, with special emphasis on its role as a pacemaker for transit of ingesta.

Gross morphology of the pelvic flexure

The pelvic flexure is a horseshoe shaped segment of the large colon joined orally to the left ventral colon and aborally to the left dorsal colon. Contrary to the other colonic flexures (sternal and diaphragmatic), it cannot be unfolded since the mesocolon attaches to its mesenteric border and holds the ventral and dorsal colon running parallel (Sisson, 1975; Ashdown and Done, 1987). It is devoid of sacculations and its mean diameter of 5.25 cm is significantly smaller than the mean diameter of 9.71 cm observed at the external flexure (Burns and
Equine colon pelvic flexure

The pelvic flexure is thus a point of narrowing of the large colon which is thought to predispose to impactions (Sellers and Lowe, 1986). The configuration of the pelvic flexure is illustrated in Figure 1.

Teniae

Teniae, or intestinal bands, are modifications of the outer longitudinal muscular layer seen in the large intestine, and contain smooth muscle and connective tissue rich in elastin and collagen fibers (Fig. 1). The pelvic flexure has only one tenia, which runs along its mesenteric border, covered by the mesocolon. At the oral portion of the pelvic flexure, the left ventral colon has four teniae symmetrically distributed around its circumference: teniae mesocolica lateralis, teniae libera lateralis, teniae libera medialis and teniae mesocolica medialis. While running aborally towards the pelvic flexure, the teniae mesocolica lateralis, teniae libera lateralis and teniae libera medialis gradually become wider and thinner, blending into the longitudinal portion of the tunica muscularis of the pelvic flexure. The remaining teniae mesocolica medialis continues through the pelvic flexure and is continuous with the tenia mesocolica ventralis of the left dorsal colon (Sisson, 1975; Burns, 1992).

Arterial supply

The arterial supply to the pelvic flexure comes from the colic branch of the ileocolic artery and the right colic artery, which are branches of the cranial mesenteric artery. The colic branch runs aborally through the mesocolon and close to the dorsal tenia of the ventral colon. In a similar fashion, the right colic artery runs orally through the mesocolon and close to the ventral tenia of the dorsal colon. The colic branch of the ileocolic artery anastomoses with the right colic artery at the pelvic flexure. While these arteries run parallel to the large colon, branches arise and run towards the intestinal wall (Smyth, 1988).

Venous drainage

The veins draining the pelvic flexure closely follow the arteries. A venous arc is formed by the anastomosis of the two main veins, which run parallel to the colic branch of the ileocolic artery and to the right colic artery, respectively. The right colic vein drains into the caudal mesenteric vein while the left colic vein drains into the cranial mesenteric vein. Both cranial and caudal mesenteric veins drain into the portal vein (Smyth, 1988; Pasquini, 1991).

Lymphatic drainage

The lymphatics of the pelvic flexure drain into the colic lymph nodes, which are multiple, small lymph nodes situated in the mesocolon. Efferents from the colic lymph nodes drain into lymph nodes located in the region of the cranial mesenteric artery and are termed, cranial mesenteric lymph nodes. Through the intestinal trunk, lymph from the cranial mesenteric lymph nodes is drained into the cisterna chyli, and then through the thoracic duct, into the cranial vena cava or into the left jugular vein (Saar and Getty, 1975).

Extrinsic innervation

The extrinsic innervation of the pelvic flexure is composed of parasympathetic fibers derived from vagal
nerves, and sympathetic fibers originating in the cranial mesenteric ganglia, which in turn receive presynaptic fibers from the thoracic sympathetic outflow (Dyce, 1958; Argenzio, 1975). In the equine large colon, large strands (about 1-3 mm diameter) originating from vagal and sympathetic nerves form a netlike layer in the adventitia of the colic arteries near their origins (Sellers et al., 1979).

**Position**

In the standing horse, the pelvic flexure is usually positioned in the left half of the abdomen in contact with the abdominal wall and close to the pelvic inlet (Sisson, 1975; Ashdown and Done, 1987). In some normal animals it can also be found situated in the pelvic cavity (White, 1998), or even deviated medially, crossing towards the right side just cranial to the pelvic inlet (Smyth, 1988). As a result of its normal propulsive movements, it may also be positioned cranial and out of reach for transrectal palpation (White, 1998).

**Histology of the pelvic flexure**

Similarly to the other intestinal regions, the pelvic flexure wall has four layers. The serosa is the most external, and is composed of a single layer of mesothelial cells covering a thin sheath of loose connective tissue. The underlying muscular layer is composed of two distinct muscular layers: the external, which has its cells aligned parallel to the longitudinal axis of the intestine, and the internal layer with its fibers aligned perpendicular to the longitudinal axis. Between the two muscular layers is the myenteric plexus (Auerbach’s plexus), which is a network of neuronal ganglia of the enteric nervous system. The subjacent submucosa is mainly composed of loose connective tissue, and contains as in most mammalian systems a submucous plexus (Meissner’s plexus), which is another network of the enteric nervous system, grouped into multiple ganglia. The innermost mucosal layer is bounded by a thin muscular layer, the muscularis mucosae, and has an extensive lamina propria covered by epithelial cells. The epithelial cells, comprised of principal cells and goblet cells, form straight glands oriented perpendicular to the luminal surface.

Many aspects of equine colonic histology have not yet been studied in detail. However, there are a few reports describing some particularities of the equine colon related to the microcirculation, the enteric nervous system and its neurotransmitters, and some morphologic aspects of the mucosa.

**Microcirculation**

The colic arteries travel parallel to the ventral and dorsal colon and small arterial branches bifurcate towards the anti-mesenteric border of the pelvic flexure. Close to their origin these small arteries form an anastomosing network, the colonic rete, surrounding the large colic vein. This network is thought to monitor changes in venous pressure, thus allowing a reflex adjustment in the arterial flow (Snyder et al., 1989).

According to Sellers et al. (1979), the anastomosis of the colonic rete protects against arterial obstructions caused by *Strongylus vulgaris* larvae migration, which is a risk factor for equine colic.

Another arterial network originating from the colonic rete supplies the mesenteric lymph nodes. Distal to the colonic rete, the arteries run toward the anti-mesenteric border, where they anastomose with the arteries from the other side. Along the way to the anti-mesenteric border many branches originate from these arteries which gradually become smaller. Approximately 3 to 4 cm from the mesentery the arterial supply penetrates the serosa and muscularis, forming an extensive submucosal plexus. The mucosa, muscularis mucosae, submucosa, muscular layers (circular and longitudinal), and serosa are supplied by the submucosal plexus. The blood supply to the mucosa comes from vessels that penetrate the muscularis mucosa. Contrary to what is seen in the small intestine, the lamina propria is devoid of vessels with a smooth muscular coat and the mucosal network is exclusively formed by capillaries (Snyder et al., 1989).

**Intrinsic inervation**

Only a few studies of the enteric nervous system of the horse have been published. Since reports of evidence of a pacemaker in the pelvic flexure (Sellers et al., 1979, 1982a,b), this segment has been the focus of several recent studies.

The presence of substance P-like immunoreactivity in the equine pelvic flexure nervous system was evaluated by Cummings and co-workers (1984). Immunoreactivity to substance P was observed in nerve fibers in all layers of the intestinal wall and in the cell bodies of the enteric nervous system, suggesting its physiologic role in the large colon. Sellers and co-workers (1985) also observed increased contractile activity and vasodilation in the pelvic flexure when the excitatory neurotransmitters, substance P and serotonin, were injected into the colic artery, documenting their role as biotransmitters in this intestinal segment.

Burns and Cummings (1991) evaluated the neuronal density of the myenteric plexus in different segments of the equine intestine. Compared to the other segments, a higher number of neurons was observed at the transition of the pelvic flexure to the dorsal colon of the equine intestine, which corroborates the hypothesis of a pelvic flexure pacemaker (Fig. 1).

In another study Burns and Cummings (1993) evaluated the distribution of four neurotransmitters in the horse intestine. The distribution of substance P, methionine-enkephalin, and calcitonin gene-related peptide (CGRP) was uniform throughout the ten tested sites. However, higher reactivity for vasoactive intestinal
Equine colon pelvic flexure

peptide (VIP) was observed at the apex of the pelvic flexure and in the left dorsal colon, which suggested an important role of this neuropeptide in the pelvic flexure pacemaker.

Schusser and White (1994) conducted a morphologic study of the equine myenteric plexus and observed a greater number of ganglia and neurons per cm in foals than in adults. Comparing the results of different intestinal segments, a higher number of ganglia and neurons per cm was seen in the pelvic flexure, left dorsal colon and transverse colon of the foals. Later, Schusser and White (1997) reported a higher density of ganglia and neurons in the pelvic flexure, left dorsal colon and transverse colon also in the adult horse.

Sonea and associates (1997) investigated the distribution of tachykinin receptors in the pelvic flexure. These receptors were plentiful in the smooth muscle layers, mainly in the mucosal and circular layers, in the blood vessels, and in the mucosa. They also noted the predominance of neurokinin-1, followed by the neurokinin-3, suggesting the possible use of highly specific tachykinin receptor agonists and antagonists to modulate pelvic flexure function.

Mucosa

The colonic mucosa (all regions) is devoid of villi but has long crypts. The mucosal surface is smooth with prominent crypt openings. Goblet cells are numerous in all regions of the equine colon and are seen both on the luminal surface and lining the glands (Pfeiffer and MacPherson, 1990). The number of goblet cells is higher in the right dorsal than in the right ventral colon (Morris, 1954; De Boom, 1975), and the crypt depth and area are increased compared to what is seen in the more proximal segments of the large intestine (Bertone et al., 1989). Goblet cells are numerous in the mucosa of the pelvic flexure (Fig. 2), but quantitative comparisons with the ventral and dorsal regions of the colon are not yet available.

The principal cells lining the ventral and dorsal colonic glands are granular cells, which are responsible for the major and rapid secretion of water and bicarbonate and phosphate buffer into the lumen, and

![Fig. 2. Electron micrograph illustrating part of the mucosal epithelium of the pelvic flexure, basal region on the left. Portions of a goblet cell with mucous granules (M), and principal cells are shown. Note the apical cytoplasmic, small granules (G) in the principal cell type, and similar electron dense granules present as intranuclear inclusions (I). x 8,800](image)
absorption of water and dietarily-derived, volatile free fatty acids (C-1 to C-3 chain length). While the mucosal surface area and luminal capacity of the colonic pelvic flexure is insignificant compared to the combined ventral and dorsal colon, some bidirectional mucosal transport undoubtedly takes place in the pelvic flexure. This has not yet been physiologically assessed. These principal cells of the large colon are often observed in mitotic stages, and have a characteristic of numerous small, apical electron dense cytoplasmic granules (Pfeiffer et al., 1987). Clusters of these granules are commonly observed also in an unusual intranuclear location. The composition, origin, and physiological role of the apical and nuclear granules remain unknown but they are evidence of both nuclear import (Pfeiffer et al., 1987) and significant luminal secretion of this undetermined product by colonic cells. The mucosal cells of the pelvic flexure (Figs. 2, 3) also contain these apical and intra-nuclear granules. The goblet cells also appear similar as elsewhere in the equine colon.

In the normal horse, the submucosa and lamina propria of the left large colon are usually infiltrated with a large number of granulocytes and mononuclear leukocytes. Eosinophils are the predominant granulocyte, but neutrophils are also found. Myeloperoxidase activity is normally high, and positively correlates with the degree of granulocyte infiltration (McConnico et al., 1999). Lamina proprial capillaries and arterioles can be observed in close proximity to small neurons in the pelvic flexure (Fig. 4).

Endocrine cells are also found in the mucosa of the pelvic flexure and as there is often overlap in composition of neurotransmitter peptides found in gut neurons as well as in gut endocrine cells, the latter may also contribute to the regulation of the equine pelvic flexure pacemaker activity. Early studies by Japanese workers (Sato et al., 1976, 1978) characterized EC, L, M, and D endocrine cell types in the equine gastrointestinal tract. However, only the EC type was present in the colon, and the pelvic flexure was not specifically assessed. L and M cell types were found in the rectum but not colon. Later studies by Kitamura and associates (1984) immunocytochemically assayed for somatostatin, gastrin, glicentin, glucagon, secretin, cholecystokinin, motilin and neurotensin in the horse alimentary tract. Only somatostatin- and glicentin-
Equine colon pelvic flexure

immunoreactive cells were noted in the colon and rectum, and were numerous. These workers did not specifically examine the pelvic flexure. Mucosal endocrine cells in the large intestine containing serotonin also appear to be involved in regulation of motility in the horse (Weyns et al., 1985).

Physiology of the pelvic flexure

According to Argenzio et al. (1974), the horse has a slow transit of ingesta through the large colon, which facilitates microbial digestion and absorption of water and electrolytes. They observed that the transit is relatively rapid from cecum to large colon, but the release of ingesta from ventral to dorsal colon is slow. They also reported that solid and liquid markers administered into the right dorsal colon were recovered in the left dorsal colon, but retrograde movement of markers into the ventral colon did not occur. Although these results suggested that the pelvic flexure was a major barrier to the flow of ingesta, no morphologic evidence of a sphincter at this site has been found.

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Sellers and associates (1979) studied the motility in

Fig. 4. Section from mucosal lamina propria of equine pelvic flexure, showing part of arteriole immediately adjacent to small non-myelinated neuron (N). The arteriolar smooth muscle cells (arrows), endothelial cell (E), and lumen (L) are evident. x 7,700
colleagues (1974), and a theoretical basis for a mechanism for large colon impaction and displacement (Sellers and Lowe, 1986). From an anatomic perspective Burns and Cummings (1991) and Schusser and White (1997) found a higher density of the myenteric plexus in the segment identified as the pacemaker region, giving more support for the pelvic flexure pacemaker theory. However, Roger et al. (1985) and Merritt et al. (1995) also monitored the electrical and motor activity at the pelvic flexure, and could not identify the pacemaker activity previously reported. Their experimental protocols were quite different and, while Sellers and colleagues (1979, 1982, 1984) based their hypothesis on only a few minutes of observations, Merritt and colleagues (1995) recorded the colonic activity for 5 hours.

The role of the pelvic flexure

Large colon impaction is one of the most commonly diagnosed maladies in horses presenting with colic (White, 1990; Cohen et al., 1999) and the pelvic flexure is the most common site for impaction formation (Dabareiner and White, 1995). It is a point of luminal narrowing, which seems to be a factor limiting the transit of ingesta, and predisposing to obstruction. Additionally, the coordinated retropropulsive contractions originating near the pelvic flexure are thought to keep the less well-digested particles in the ventral colon, also contributing to impaction formation.

Obviously, a further narrowing of the relatively small lumen of the pelvic flexure, caused by any pathologic process, could lead to obstruction (Sellers and Lowe, 1986), although this has not been commonly reported. Congenital adhesions resulting in abnormal configuration of the pelvic flexure were thought to cause recurrent impaction and colic in a gelding (Suann and Livesey, 1986). Impaction secondary to pelvic flexure stricture caused by annular fibrosis has been reported in two horses. These findings suggested a healing response, although in no case was the primary insult identified (Rose et al., 1991). The occurrence of peritoneal adhesions to the pelvic flexure has been reported to cause impaction in a filly with peritonitis. Laparoscopic dissection of the adhesions relieved the pelvic flexure and allowed the return of normal transit (Boure et al., 1998).

Amitraz toxicosis has been associated with large colon impaction (Roberts and Seawright, 1983). According to Sellers and associates (1982a,b), it caused a disassociation of electrical and motor events between the left ventral colon and left dorsal colon, producing ileus. This amitraz disruption of normal function of the pelvic flexure pacemaker can be blocked by the alpha-2 adrenergic antagonist, yohimbine, suggesting that amitraz has an alpha-2 adrenergic agonist activity (Sellers et al., 1985).

Recently, Schusser and White (1997) reported a reduced number of neurons in the myenteric plexus of the pelvic flexure in horses with large colon impaction. They also found evidence of ganglionitis and neuronal degeneration in horses with acute, colonic obstruction and strangulation. These observations suggested that acute injury to the myenteric plexus, produced during obstruction or strangulation, could permanently reduce its neuronal density, compromising the function of the pelvic flexure pacemaker and causing impaction. This hypothesis agrees with the higher incidence of colic in horse with a history of previous large colon impaction, as reported by Dabareiner and White (1995).

Large colon displacement and torsion are also commonly reported in horses (White, 1990; Cohen et al., 1995). According to Sellers and Lowe (1986) these maladies could be caused by a malfunction of the pelvic flexure pacemaker. The motility pattern coordinated by the pelvic flexure pacemaker normally produces shortening of the left colon moving the pelvic flexure toward the diaphragm, followed by backward movement toward the pelvis during relaxation. Hence, it is conceivable that changes in this motility pattern could result in displacements and torsion.

The occurrence of cranial displacement of the pelvic flexure secondary to peritoneal adhesions was reported in one horse. Previously, this animal had been subjected to laparotomy to correct a left dorsal displacement of the large colon. The adhesions resulted from the inflammatory process associated with colonic injury caused by the colon entrapment and/or surgical trauma. Surgical resection of the adhesion allowed appropriate repositioning of the pelvic flexure (Markel et al., 1985).

Pelvic flexure enterotomy is a common procedure in cases of large colon impaction and enterolithiasis, and it allows access to both ventral and dorsal compartments of the large colon. Most often healing proceeds uneventfully, but peritoneal adhesions or stricture can form, leading to the malfunctions previously discussed. In order to prevent postsurgical complications, appropriate surgical techniques must be used. A longitudinal incision on the anteilesmental side of the pelvic flexure is recommended. The enterotomy should be closed in two layers with synthetic absorbable suture and a full thickness, simple continuous suture oversewn with the Cushing seromuscular pattern (Young et al., 1991).

Conclusions

Although numerous details of the complex features of colonic morphology and physiology have been described in non-equine species (Johnson et al., 1994), extrapolation from these different species to the horse is hazardous at best (Argenzio, 1982). Considering the unique features of the equine digestive system, especially its hindgut, and the common occurrence of gastrointestinal disease in the horse, it is clear that much more investigation in this species is needed. The study of colonic motility patterns and in particular the role of the pelvic flexure is required in order to understand equine...
colonic physiology better, and will also contribute to elucidating the pathophysiology of large colon, i.e., displacements and impactions. The role of the pelvic flexure pacemaker plays a significant though poorly understood part in the function.

References


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