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TISSUES AND ORGANS OF THE IMMUNE SYSTEM OF DROMEDARY CAMEL (*Camelus dromedarius*): A COMPARATIVE REVIEW

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ABSTRACT

The immune system is formed of sets of tissues and organs that have the ability to discern self-substances from non-self (antigen) substances and to destroy or inactivate the latter. This review presents a literary survey of what has been written on the subject of the histology of the immune system in dromedary camels and compared the structure of these tissue and organs to that of ruminants.

Key words: Camel, comparative, histology, immune, organs, system, tissue

Camelids, until now, considered as a case of evolutionary innovation, represent a new mammalian model particularly useful for understanding the role of diversity in the immune system function. Studies on selected aspects of camel immune system and immune responses has been done. The anatomical and histological details of the camel's immune organs have shown a structure which differs from other ruminants, in particular the thymus, tonsils, and peyer's patches (Al-Ramadan *et al,* 2021). Camels show strong resistance to many viral and microbial infections, including tetanus, foot-and-mouth disease and mad cow disease (or bovine spongiform encephalopathy) which is attributed to its special immune system (Jassim and Naji, 2001).

A compilation of research on camel immune system; determinates of innate immunity, cells, organs and tissues of immune system; antibodies; immunomodulation; histocompatibility; sero-prevalence, diagnosis and immunity against infections; application of camel immunoglobulins and applications of immune mechanisms in physiological processes is published (Gahlot *et al,* 2016).

Some research and review papers have been published recently on the camel's immune system (Al-Ramadan *et al,* 2021; Hussen and Schuberth, 2021). However, there is no organised compilation of the microscopic structure of all known tissues and organs of the immune system. Therefore, this paper is aimed to project an overview of the histological characteristics of different tissues and organs of the immune system of dromedary camel.

The tissues and organs of the immune system of dromedary camel are described as the central and peripheral lymphatic organs.

The Central Lymphatic Organs

These organs are referred to as the primary lymphoid organs where the lymphocytes develop and mature.

Bone Marrow:

The bone marrow is where pluripotent haematopoietic stem cells reside (Gurkan and Akkus, 2008). In addition to its function as a generator for blood cells, bone marrow represents the antigen independent phase of B-lymphocyte development in many animal species (Boes and Durham, 2017). Paradoxically, despite the importance of the marrow for immunity, the camel's bone marrow has not been studied in-depth compared to other species. The procedure goes through several complex steps, including decalcification of the bone, which has made many investigators reluctant to study the bone marrow *in situ* and use bone marrow aspiration instead. However, the bone marrow is formed of haematopoietic cells, fat cells, blood vessels, and a connective tissue framework. The haematopoietic cells occur in various stages of formation and maturation (Travlos, 2006; Samuelson, 2007; Boes and Durham, 2017). A network of sinusoidal capillaries permeates the myeloid tissue of bone. These blood sinusoids are wide, irregular vessels, the walls of which consist of fenestrated endothelium, thin basal lamina, and

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some scattered adventitia, allowing the newly formed cells to squeeze between the spaces to and from circulating blood. The framework of bone marrow is represented by reticular cells, osteogenic cells, and fat cells. The reticular cells are branched cells with large pale nuclei, while the osteogenic and fat cells have ordinary cell structure (Travlos, 2006; Samuelson, 2007).

Smears taken from bone marrow showed that the mean myeloid/erythroid ratio was 1.21. In percentiles, the mean erythroid percentage was 42.7%, and the mean myeloid percentage was 52.0%; the percentage for other cell types was 5.2% (Nazifi *et al,* 1998).

Thymus Gland:

Thymus gland originates from the 3rd and 4th pharyngeal pouches and descends to ventral part of the cervical region, thoracic inlet, and cranial mediastinum as a bilobed organ. The thymus gland started as an epithelial structure; during its ontogenesis, it was infiltrated with lymphocytes that originated in the bone marrow (Varga *et al,* 2011). As more lymphocytes accumulated in thymus, the epithelial cells became loosely arranged in the reticulum and are called epithelial-reticular or epithelioreticular cells; hence, the thymus gland is described as a lymphoepithelial organ (Roballo *et al,* 2019).

In dromedary camel, the thymus gland descended back and finally positioned itself at the ventral aspect of the neck and the thoracic cavity, at the anterior superior mediastinum in front of the heart and behind the sternum (Jarrar and Faye, 2013). It might extend to the caudal fourth segment of the neck, where it can be seen between the trachea and left external jugular vein (Smuts and Bezuidenhout, 1987; Al-Ramadan *et al,* 2021). In dromedary camel, a thin connective tissue capsule surrounds the thymus gland. Arising from the capsule, thin connective tissue trabeculae extend deeply into the parenchyma, dividing the lobes into incompletely separated lobules. The thymic lobules have irregular outlines, and each consists of an outer dark cortex and inner light medulla (Fig 1).

The cortex is highly populated by T-lymphocytes (thymocytes), rendering this peripheral part of the lobule darkly stained. In addition to T-lymphocytes, epithelioreticular cells could be detected in the camel's thymus gland. However, these cells were highly outnumbered by thymocytes, and they had a stellate-shape with extending cell processes (Jarrar and Faye, 2013). This histological appearance in the dromedary camel has also been reported in other domestic animals where the thymic lobule has a distinct medulla and cortex. The cortex has been described as densely packed with small lymphocytes, rendering the cortex darkly stained, while the medulla is occupied by fewer lymphocytes and is thus lightly stained (Aughey and Frye, 2001). Within the medulla, acidophilic bodies 20–100 µm in diameter could be detected. These structures are called thymic corpuscles and are composed of concentric whorls of epithelioreticular cells (Pearse, 2006; Samuelson, 2007). As with the camel, the epithelioreticular cells are irregular with large branching cytoplasmic processes. These processes connect to each other by means of desmosomes, forming a blood-thymus barrier (Aughey and Frye, 2001). Moreover, the epithelioreticular cells have large, oval, lightly stained nuclei (Banks, 1993). In cattle calves, the lobules are surrounded and interconnected by interlobular connective tissue that contains blood and lymph vessels (Gasisova *et al,* 2016). In camel, however, although a similar description has been mentioned, numerous granulated cells of different shapes and sizes were observed in the interlobular connective tissue and occasionally adjacent to the cortex (Ismail and Ali, 2015). According to morphology and function, two distinct types of lobules have been identified: (a) passive and (b) active; the active lobules are larger and have a clear demarcation between the cortex and medulla. In addition, they differ from each other by cell density and mitotic activity (Gasisova, 2016). No such description has been found in the camel except for the ordinary description of thymic lobules as having a dark cortex and lightly stained medulla (Ismail and Ali, 2015).

The Peripheral Lymphatic Organs

Mucosal Associated Lymphatic Tissue (MALT)

Sporadic unencapsulated lymphatic tissue:

These cells are scattered throughout the body, mainly in the connective tissues of mucous surfaces. Their presence is more noticeable in the organs of digestive, respiratory, and urogenital systems that are continually subjected to noxious agents. This lymphoid tissue appears as a rather loose aggregate of cells and shows no distinct demarcation from the surrounding tissue with which it gradually merges (Cesta, 2006). According to the anatomical location, several groups of MALT have been described (Casteleyn *et al,* 2011a; 2011b; Girgiri and Kumar

2020). The two groups most extensively described are bronchus-associated lymphoid tissue (BALT) and gut-associated lymphoid tissue (GALT). However, conjunctiva-associated lymphoid tissue (CALT) and teat-associated lymphoid tissue have also been described (Casteleyn *et al,* 2011a).

BALT

Bronchus associated lymphoid tissue is not a constitutive structure in all domestic animal species. While it is absent in dogs (Peeters *et al,* 2005), it has been reported in sheep (Liebler-Tenorio and Pabst, 2006; McNeilly *et al,* 2008), goats (Rodriguez *et al,* 2001; Choudhary and Das, 2019), cattle (Chase and Kaushik, 2019), and equines (Hannant, 2002; Liebler-Tenorio and Pabst, 2006). In this consideration, Patches of lymphocytic aggregations represent BALT in the camel are formed of lymphoid nodules that are scattered along the bronchial tree in the entire lung. These are of variable sizes and seen under the epithelial lining of bronchi and bronchioles in the lamina propria and submucosa (Fig 2) (Elhussieny *et al,* 2017).

Recently, Elhussieny and Zidan (2021) provided temporospatial characteristics of BALT in the dromedary camel. BALT of the extrapulmonary bronchi of young camels (younger than 2 years) was rarely detected. In middle-aged camels (from 3 to 7 years), however, BALT was represented by well-developed nodular and diffuse internodular lymphocytes, which involuted in camels older than 12 years to be in the form of a few diffusely distributed lymphocytes. BALT of intrapulmonary bronchi of young and middle-aged camels was very well developed and formed of organised lymph nodules and internodular lymphocytes. In older age camels, BALT was faded out, and only few lymphocytes were detected in the lamina propria (Fig 2) (Elhussieny and Zidan, 2021).

In this respect, BALT of the Bactrian camel is represented by isolated aggregates of lymphoid nodules in the bronchial tree. However, the density of BALT increased from trachea to the lower graded branches where most density was seen at bronchioles, which then decreased at the level of respiratory bronchioles (He *et al,* 2019). In bovines, both organised lymphoid nodules and unorganised aggregates of lymphocytes were seen in the bronchi as well (Liebler-Tenorio and Pabst, 2006). Whereas, BALT of young goats was represented by aggregations of lymphocytes that were seen in diffused form rather than nodular form (Choudhary and Das, 2019), BALT could not be detected in the neonatal goats (Barman *et al,* 1996). The authors suggested that the absence of any lymphoid tissue in the bronchial tree in the neonatal goats and the presence of it at later ages suggest postnatal evolution of BALT similar.

GALT

GALT comprises diffuse and isolated lymphoid nodules that are scattered throughout the intestinal tract (Cesta, 2006). However, in some locations, the nodules in the gut aggregate to form patches, which will be discussed in the section on nodular lymphatic tissue because of their immunological significance.

With the exception of pigs, gastric GALT is not very well developed as in other farm animals (Liebler-Tenorio and Pabst, 2006; Mazzoni *et al,* 2011). Gastric GALT in Bactrian camels has been described in several publications (Wang, 2003; Xu *et al,* 2010; Zhang *et al,* 2012a); in dromedary camels, the gastric lymphoid tissue was reported only in the 4th compartment of the stomach (Naser *et al,* 2011). The latter authors could detect several lymphoid nodules with massive cellular components at the pyloric region of the fourth compartment (Fig 3).

In this respect, the gastric GALT in Bactrian camel was located only in the cardiac glandular area of the 3rd stomach compartment, forming a long triangle-like region, and distributed along the ventral walls of the stomach neck, the beginning of the cranial enlargement, and along the lesser curvature, forming lymphoid nodules (Wang, 2003; Gahlot *et al,* 2016). However, Xu *et al* (2010) and Zhang *et al* (2012a) found that the number of these nodular aggregations changed with age, with peak at the age of puberty and decreasing as the animals aged. A large number of lymphocytes in the form of lymphoid aggregations were observed in torus pyloric region of the caprine abomasum (Mahesh *et al,* 2017).

CALT

In the camel, CALT was detected at the palpebral surface of the eyelids in the form of several lymphoid follicles. These follicles formed aggregates near the medial canthus (Al-Ramadan and Ali, 2012; Al-Ramadan, 2015) and morphologically appeared as basophilic patches of a single follicle or as a group of two or more nodules (Fig 4). CALT is a constant component of conjunctiva of several domesticated animals. The CALT is formed of solitary or aggregates of lymphoid nodules in Bactrian camel (Yang and Wang, 2015; Gahlot *et al,* 2016). In cattle, sheep, and pigs, isolated lymphoid nodules that were

predominantly localised at the palpebral surface of the conjunctiva represent the CALT (Chodosh *et al,* 1998.

Nodular lymphatic tissue:

Populations of lymphatic nodules are organised into compact, somewhat spheroidal or oval structures of MALT. It may occur anywhere in connective tissue but is prominent along the digestive and respiratory tracts. In mammals, some of these nodule aggregations at locations such as pharynx are called tonsils, and in the small intestine called Peyer's patches or intestinal tonsils (Banks, 1993; Liebler-Tenorio and Pabst, 2006; Samuelson, 2007).

Tonsils:

Tonsils are aggregates of lymphatic nodules at the entrance of digestive and respiratory systems. The surface facing the cavity is covered by irregular epithelium, and underneath these are partially encapsulated with dense connective tissue. The epithelial irregularities could be in the form of crypts or sinuses, resulting in two classes of tonsils: (a) tonsils with crypts, which have deep invagination of the surface epithelium, and (b) tonsils without crypts (Banks, 1993; Casteleyn *et al,* 2011b). Further classification based on the anatomical locations of tonsils has classified the tonsils into three groups: (a) oropharynx tonsils, (b) nasopharynx tonsils, and (c) laryngopharynx tonsils. The oropharynx group is formed of lingual, palatine, and velar (soft palate) tonsils; the nasopharynx tonsils are subdivided into the pharyngeal and tubal tonsils; and the laryngopharynx type is formed of the paraepigllotic tonsil only (Cocquyt, 2008; Perry and Whyte, 1998). In a comprehensive study using the dromedary camel, Achaaban *et al* (2016) described tonsils within each of the 3 groups.

Oropharynx group:

A. *Palatine tonsil:* This tonsil could be described as comprising spherical masses located within a tonsillar fossulae and extending between the palatoglossal and palatopharyngeal arches. Microscopically, these spherical masses consist of a large number of lymphatic cells arranged into heavily cellular ovoid or spherical nodules and internodular areas. The mucous membrane covering the palatine tonsil is formed of a thick layer of nonkeratinised stratified squamous epithelium. As shown in Fig 5, the epithelium is reflected inside the tonsil, forming a blind-ended crypt that is usually infiltrated with lymphocytes to form reticular epithelium (Zidan and Pabst, 2009; Achaaban *et al,* 2016; Al-Ramadan and Alluwaimi, 2018). In the Bactrian camel, this tonsil is very similar to that of the dromedary camel, except that the crypt in the Bactrian camel is often branched with wide lumen (Yang *et al,* 2011). The palatine tonsil of cattle is formed of a large ovoid lymphoid structure with a central sinus, giving the tonsil a bean-shaped appearance with an entrance visible at the oropharyngeal surface (Effat and Milad, 2007; Casteleyn *et al,* 2011a). Opening into this tonsillar sinus are numerous crypts in the center between the tonsillar nodules. More than one sinus could be detected in the palatine tonsil of bovines (Casteleyn *et al,* 2011a). Similar to that in camel, the crypt in bovines comprises nonkeratinised stratified squamous epithelium and is often infiltrated by lymphoid cells (Velinova *et al,* 2001; Liebler-Tenorio and Pabst, 2006; Palmer *et al,* 2009; 2011). The palatine tonsil of sheep is a hazelnut-sized ovoid structure that could be detected at both sides of the oropharynx. This tonsil has 1 to 3 entrances between the palatoglossal and palatopharyngeal arches. Each one of the entrances leads to the underlying crypts. In turn, these crypts are centrally located between the lymphoid nodules (Cocquyt *et al,* 2005; Casteleyn *et al,* 2011a). Within the crypts is overlying nonkeratinised stratified squamous epithelium. The epithelium is irregularly modified into a reticular epithelium as a result of heavy infiltration by lymphoid cells (Casteleyn *et al,* 2011a). In goats, the palatine tonsil is larger than that in sheep. It is easily detected at the lateral oropharyngeal wall. Moreover, it is characterised by few crypt openings leading to large diverticula (Indu *et al,* 2018). The lymphoid tissue of goat tonsils is formed of many secondary follicles and interfollicular lymphoid tissue. The tonsil is covered by nonkeratinised stratified squamous epithelium, and the epithelium that lines the crypt is transformed into follicle-associated epithelium, which is characterised by the absence of goblet cells and cilia, a reduced number of cell layers, and infiltration of a large number of lymphocytes (Casteleyn *et al,* 2011a).

B. *Lingual tonsil:* This tonsil is located at the root of the tongue and made up of a cluster of spheroidal lymphoid masses which protrude into the oropharynx. Achaaban *et al* (2016) and Zidan and Pabst (2020) agreed that the lingual tonsil in dromedary camel is visible at the root of the tongue as several spherical macroscopic nodules protruding into the oropharynx; however, they disagreed about the presence of the crypt of this tonsil. Achaaban

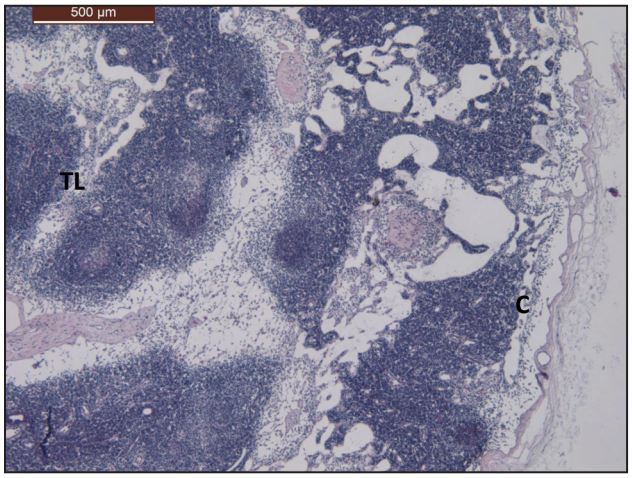

Fig 1. Thymus gland of dromedary camel showing capsule (C), Thymic lobule (TL) (H&E). Bar= 500µm.

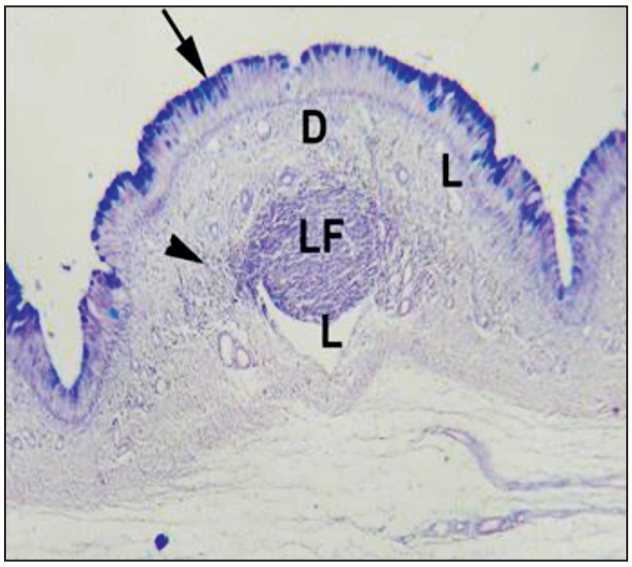

Fig 2. The BALT of the extrapulmonary bronchus is localised in dome like area (D) and formed from lymphoid follicle (LF) and diffused lymphocytes (arrowhead). The covering epithelium (arrow) is rich in goblet cells. L= lymphatics. Alcian blue- PAS stain. (El-hussainy *et al,* 2017).

et al (2016) mentioned that the crypt is not clearly visible in the lingual tonsil of the dromedary camel, but Zidan and Pabst (2020) described more than one crypt in the dromedary camel's lingual tonsils. Microscopically, lingual tonsil dromedary camel consisted of a cluster of lymphoid nodules and internodular tissue. These nodules were covered by a keratinised stratified squamous epithelium continuous with similar epithelium of the lingual surface (Fig 5). In this respect, Yang *et al* (2011) found that lingual tonsil of the Bactrian camel is formed of aggregations of lymphoid cells at the dorsum of the tongue, extending 2 cm rostral to last vallate papilla on each side. In bovines, the lingual tonsil is

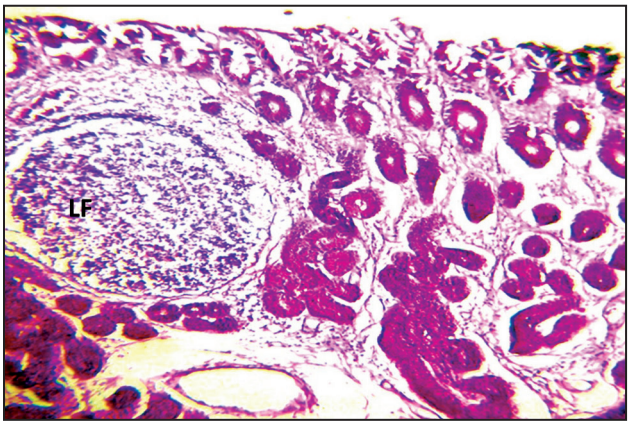

Fig 3. GALT, Lymphoid Follicle (LF) at the submucosa of the fourth compartment of camel stomach. (PAS stain). (Naser *et al*, 2011).

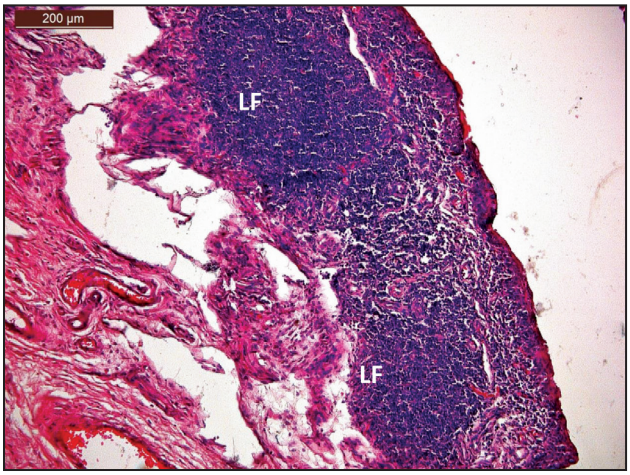

Fig 4. Conjunctiva of camel showing lymphoid follicles (LF) in the lamina propria. (H&E; bar = 200 µm). (Al-Ramadan, 2015).

represented by macroscopic rows of tonsillar fossules at the dorsolateral surface of the tongue's root, caudal to the circumvallate papillae (Liebler-Tenorio and Pabst, 2006; Cocquyt *et al,* 2008; Breugelmans *et al,* 2011; Casteleyn *et al,* 2011a). Moreover, the lingual tonsil of cattle is organised in the form of lymphoid nodules and internodular regions around crypts (Breugelmans *et al,* 2011). However, some aggregations of lingual lymph nodules without crypts have also been detected in cattle (Cocquyt *et al,* 2008). The crypt is covered by keratinised stratified squamous epithelium, which is often infiltrated by lymphoid cells (Casteleyn *et al,* 2011a). In contrast to camels and cattle, the lingual tonsil of sheep is not grossly visible, but small aggregates of lymphoid tissue could be detected at both sides of the dorsal part of the tongue (Cocquyt *et al,* 2005). In addition, Casteleyn *et al* (2011a) described some lymphoid tissue dispersed within the core of the vallate papillae

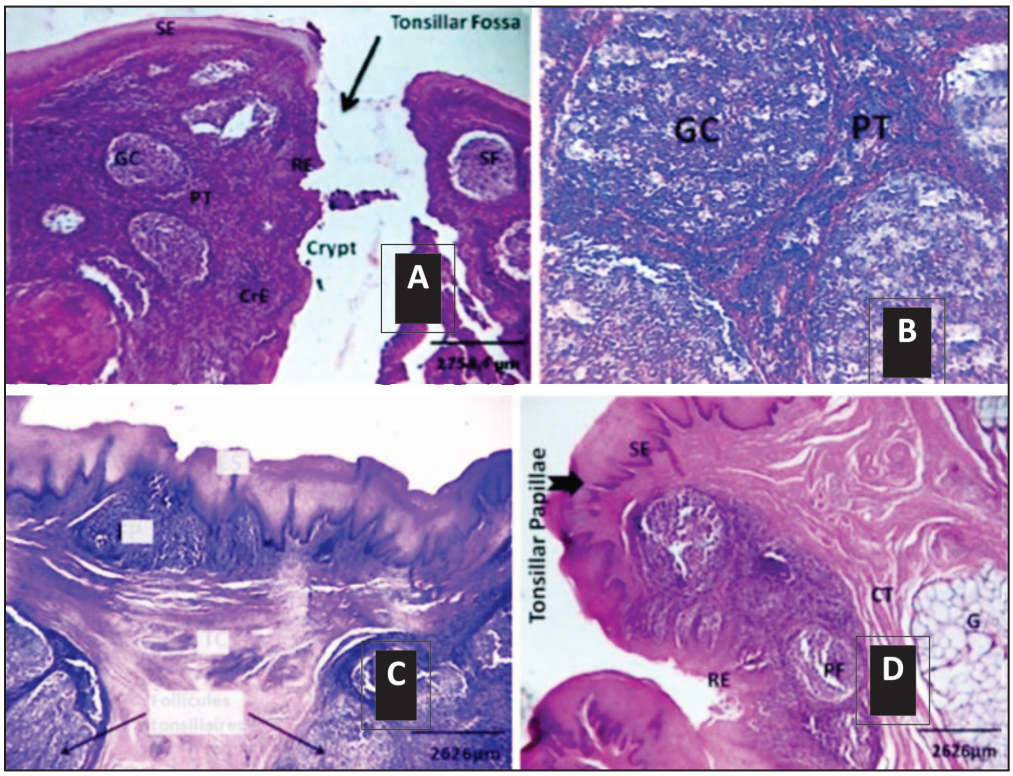

Fig 5. Tonsils of camel: (A & B) palatine tonsil; (C&D) Lingual tonsil: showing squamous epithelium (SE), primary follicle (PF), secondary follicle (SF), parafollicular tissue (PT), germinal center (GC), lingual gland (G), reticular epithelium (RE), connective tissue (CT), and crypt epithelium (CrE). (H&E) (Achaaban *et al*, 2016).

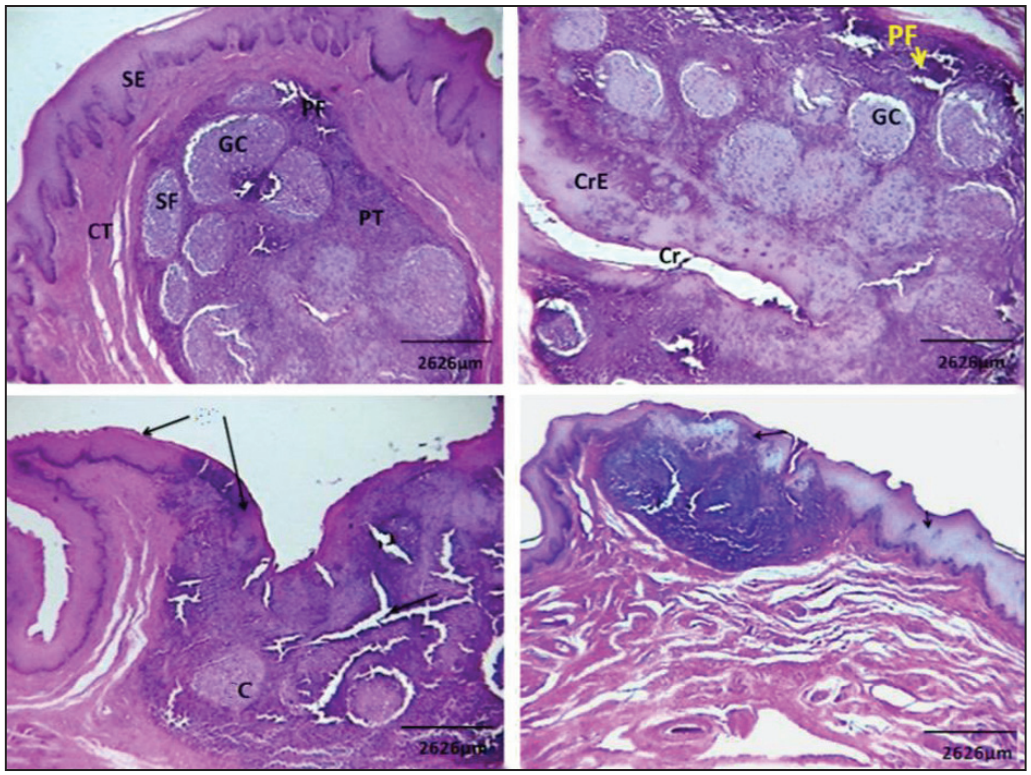

Fig 6. Velar tonsil of camel showing squamous epithelium (SE), primary follicle (PF), secondary follicle (SF), parafollicular tissue (PT), germinal centre (GC), lingual gland (G), connective tissue (CT), crypt (Cr) and crypt epithelium (CrE). (H&E) (Achaaban *et al*, 2016).

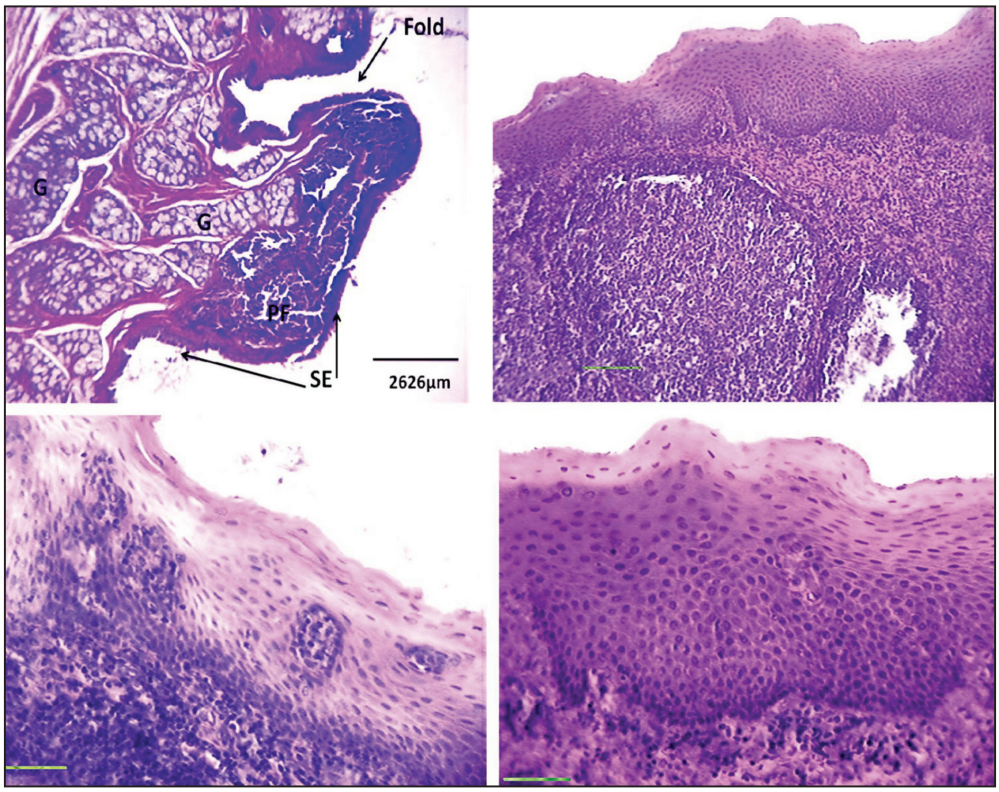

Fig 7. Tonsils of camel: Pharyngeal tonsil of camel showing squamous epithelium (SE), primary follicle (PF), secondary follicle (SF), parafollicular tissue (PT), pharyngeal gland (G). (H&E) (Achaaban *et al*, 2016).

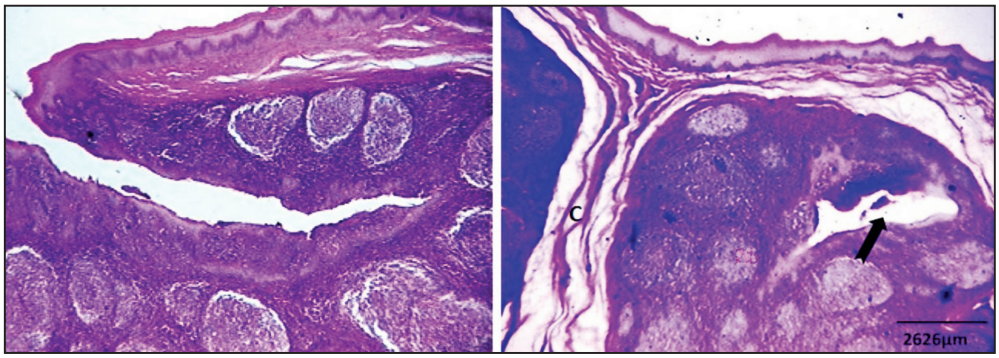

Fig 8. Tonsils of camel: Paraepiglotic tonsil of camel showing squamous epithelium (SE), secondary follicle (SF), parafollicular tissue (PT), reticular epithelium (RE), crypt fossulae (arrow). (H&E) (Achaaban *et al*, 2016).

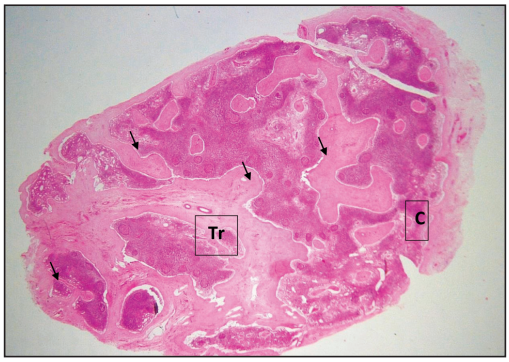

Fig 9. Lymph node of camel showing capsule (C), Trabeculae (Tr) lymphoid nodules (arrows). Dissecting microscope (H&E).

and the location of the caprine lingual tonsil at the root of the tongue disseminated from just underneath the lingual epithelium through the lingual muscle. Some lymphoid tissue was detected with connective tissue core of the vallate papillae (Casteleyn *et al*, 2011a). However, the conventional description of the tonsil is not applicable to lingual tonsil of the small ruminants that have only small aggregations of lymphoid cells that do not form lymph nodules (Casteleyn *et al,* 2011b).

C. *Velar (soft palate) tonsil:* This tonsil is located at the oropharyngeal (oral) surface of the soft palate. It is found more densely in area close

to the junction with hard palate (Achaaban *et al,* 2016). Microscopically, the velar tonsil is formed of small disseminated nodules. These nodules could be differentiated into primary (without a germinal center) and secondary (with a germinal center). The lymphoid nodules are separated by paranodular lymphoid tissue and are distributed within the connective tissue of the soft palate. Moreover, the velar tonsil is covered by keratinised stratified squamous epithelium (Achaaban *et al,* 2013; Achaaban *et al,* 2016). A crypt lined with a nonkeratinised stratified squamous epithelium has been described in this tonsil as well (Fig 6). The crypt is infiltrated with some lymphoid cells (Achaaban *et al,* 2016). In contrast to the dromedary camel, the Bactrian camel showed no macroscopic signs of velar tonsil at the oral surface of the soft palate, although it was visible after treating the soft palate with acetic acid on the aboral (nasopharyngeal) surface (Yang *et al,* 2011). Accordingly tonsil is formed of scattered lymphoid nodules that might number up to 150. In cattle, diffuse primary and secondary lymphoid follicles and interfollicular lymphoid tissue represent the velar tonsil. Similar to in the Bactrian camel, these lymphoid structures are located on the aboral surface of the soft palate underneath the respiratory epithelium (Casteleyn *et al,* 2011a). In sheep, the lymphoid tissue of the velar tonsil is unequally disseminated on the subepithelial tissue of the oral and aboral surfaces of the soft palate. While the lymphoid cells form dense aggregations on the aboral surface of the soft palate, the velar is represented by very few lymphoid cells on the oral surface (Casteleyn *et al,* 2007; Girish *et al,* 2020). Similar to cattle, the caprine velar tonsil was detected on the aboral surface of the soft palate only, where it presented in the form of primary or secondary lymphoid nodules; no aggregation of lymphoid tissue has been detected on the oral surface (Casteleyn *et al,* 2011a; Indu and Lucy, 2016).

The nasopharynx group

A. *Pharyngeal tonsil:* In the dromedary camel, this tonsil is located within the median part of the dorsal wall of nasopharynx behind the nasal septum. The tissues of this tonsil are arranged as a set of epithelial foldings, which are more like crypts. Histologically, this tonsil is formed of lymphoid nodules with diffuse lymphocytes in-between. Keratinised stratified squamous epithelium is present over this tonsil (Fig 7) (Achaaban *et al,* 2016). Likewise, the pharyngeal tonsil of the Bactrian camel is represented by a large number of primary and secondary lymphoid nodules on the caudal part of the pharyngeal septum. Over this tonsil in the Bactrian camel is folded keratinised stratified epithelium (Yang *et al,* 2011). Conversely, Casteleyn *et al* (2011a) mentioned that the pharyngeal tonsil in bovines is large, and the mucous membrane that covers this tonsil forms several folds and sometimes forms crypts. Microscopically, the lymphoid tissue consists mainly of secondary lymphoid nodules separated by internodular lymphoid tissue. This lymphoid tissue is organised around a central connective tissue core. The pseudostratified columnar ciliated epithelium is often reticulated because of infiltration by lymphocytes (Casteleyn *et al,* 2011a). Among the other tonsils, the pharyngeal tonsil is considered to be the largest tonsil in sheep (Breugelmans *et al,* 2011; Girish *et al,* 2020). It is formed of numerous lymphoid nodules and a large internodular zone and is covered by pseudostratified columnar ciliated epithelium arranged in longitudinal folds (Breugelmans *et al,* 2011; Casteleyn *et al,* 2011a). Similar to in bovines, deeper within the sheep pharyngeal tonsil, there is a connective tissue core rich in blood and lymph vessels (Casteleyn *et al,* 2011a). In this respect, the caprine pharyngeal tonsil is similar to that of sheep in terms of location and structure (Casteleyn *et al,* 2011a).

B. *Tubal tonsil:* This tonsil could be detected at both lateral walls of the nasopharynx, close to the opening of the auditory tube. Dorsally, tubal tonsil continues with the pharyngeal tonsil (Achaaban *et al,* 2016). Histologically, it is formed of lymphoid nodules, which could be detected beneath the folding squamous epithelium, similar to that observed in the pharyngeal tonsil, while the nonnodular part was arranged within the epithelial folds of nasopharynx (Achaaban *et al,* 2016). As a result of its location, the tubal tonsil is often confused with the pharyngeal tonsil (Achaaban *et al,* 2016), which might be the reason that tubal tonsil was not detected in the Bactrian camel, as mentioned by Yang *et al* (2011). Similar to the dromedary camel, the tubal tonsil in cattle is macroscopically distinguishable and microscopically consisted of primary and secondary lymphoid nodules and internodular lymphoid tissue (Casteleyn *et al,* 2011a). Only after 4 hours fixation could this tonsil be seen in sheep (Casteleyn *et al,* 2011a). However, other authors have mentioned that the nasopharyngeal tonsil consists of a raised mass covered with irregular epithelium that is deeply furrowed, but they did not specified whether it was pharyngeal or tubal tonsil (Kumar and Nagpal, 2007). Microscopically, the lymphoid tissue of the tubal

tonsil was scattered and varied from aggregated lymphoid cells to primary and secondary lymphoid follicles (Casteleyn *et al,* 2011a). Similar to sheep, this tonsil is not visible in fresh specimens from goats; however, primary and secondary lymphoid follicles and diffuse lymphoid tissue containing scattered lymphoid cells were observed on histological examination (Casteleyn *et al,* 2011a; Indu *et al,* 2015).

Laryngopharynx group

Paraepiglotic tonsil: In dromedary camels, this tonsil is situated on both sides at the base of the epiglottis. It forms circular clustered lymphoid nodules with crypt. This tonsil is formed histologically of smaller aggregates of lymphoid nodules molded together (Fig 8), constituting a very compact tonsil (Yang *et al,* 2010; Achaaban *et al,* 2016). In the Bactrian camel, this tonsil is readily located at a similar location as that of the dromedary camel. Yang *et al* (2010; 2011) mentioned that the paraepiglotic tonsil consisted mainly of secondary lymphoid nodules encapsulated in dense connective tissue. Each tonsil formed of up to 3 to 8 nodules shared 2 to 3 entrances which leads to crypts. These lymphoid tissue might serve as a connection between tonsil and BALT (Yang and Wang, 2013). In cattle, this tonsil could not be detected before immersing the laryngeal tissue in 2% acetic acid for 24 hours (Casteleyn *et al,* 2008a). However, a few lymphoid nodules could be detected microscopically that did not form aggregates. In sheep, the paraepiglotic tonsil has a similar location to that in the dromedary camel, and the nodular tissue of this tonsil could be seen as mucosal elevations separated by deep invaginations. Microscopically, it consisted of dense aggregations of lymphoid cells and primary and secondary lymphoid nodules (Casteleyn *et al,* 2011a). In contrast to sheep, this tonsil was found only in a minority of goats at the microscopic level. When it was present, it contained primary and secondary lymphoid nodules separated by internodular regions (Casteleyn *et al,* 2011a).

Peyer's Patches:

Peyer's patches (PP), also called intestinal tonsils, are aggregations of lymphoid nodules located along the antimesenteric side of the small intestine. The number, size, and distribution of PP vary according to species. In term of PP distribution, animals have been categorised into 2 groups. Group 1 includes species in which the PP are distributed all over the intestine in an unequal manner, and PP are much more numerous in ileum than in any parts of the intestine. This group includes cattle, sheep, goats, horses, pigs, and dogs. In Group 2, however, the PP are equally distributed between the jejunum and ileum, as in rabbits and rodents (Alluwaimi *et al,* 1998). In the dromedary camel, the presence of PP is confined to the ileum only (Zidan and Pabst, 2008). However, isolated follicles could be detected microscopically, which might compensate the function of jejunal PP in other species. Brandtzaeg and Pabst, 2004 and Zidan and Pabst, 2008). In this respect, PP of the Bactrian camel were detected in 3 parts of the small intestines and extended behind down to the colon (Qi *et al,* 2011; Zhaxi *et al,* 2014).

In young dromedary camels, the PP were cup-shaped masses elevated about one cm above the luminal surface. Each of these masses was formed as an aggregate of lymphoid nodules located in the submucosa, some of which extended deeply to the lamina propria. These nodules were distributed around the lateral borders and the bottom of the patches (Alluwaimi *et al,* 1998). The number of nodules per patch ranged between 25 and 27 in the cranial portion and 31 to 38 in the caudal portion. The diameters of nodules ranged between 500 and 900 µm. In adult dromedary camel, the number and size of PP were less than that of young camels (Alluwaimi *et al,* 1998). However, in a later study, Zidan and Pabst (2008) could not find any age-related variation. As is the case with other domestic species, the mucosa covering the PP was devoid of any intestinal villi (Alluwaimi *et al,* 1998; Soni *et al,* 2006).

In the Bactrian camel, four different types of PP have been described: (a) nodular, (b) faviform, (c) cup-shaped, and (d) cystic form (Qi *et al,* 2011). The nodular type has been detected in the duodenum. The faviform-shaped PP were located at the jejunum and first part of the ileum. The cup-shaped PP were mainly distributed in the mid-portion of ileum. The cystic form PP were distributed in the distal portion of the ileum (Qi *et al,* 2011).

According to Yasuda *et al* (2002) and Beyaz and Asti (2004), two types of PP were recognised in small intestine of cattle: (a) the jejunal (JPP) and (b) the ileal (IPP). In bovines, JPP were represented by several patches that could be seen along the antimesenteric side of the jejunum, while the IPP were represented by a single long patch that might reach up to 3 metres (Liebler-Tenorio and Pabst, 2006). The lymphoid nodules of JPP were small and pear-shaped with extensive internodular areas and domes. The IPP, however, had long, oval lymphoid nodules and narrow internodular areas (Liebler-Tenorio and Pabst, 2006). A similar distribution and histological

appearance to that of cattle were reported in small ruminants (Liebler-Tenorio and Pabst, 2006).

The lymph nodes:

The lymphatic centers:

The lymph nodes are grouped into lymph centers that constantly occur in same region of the body. The centres of lymph nodes in the dromedary camel could be topographically grouped as follows: (a) lymph nodes of the head, including parotid, the mandibular, and retropharyngeal lymph centers; (b) lymph nodes of the neck, including superficial and deep cervical lymph centers; (c) lymph nodes of front limb, including axillary lymph center; (d) lymph nodes of thorax, including dorsal thoracic, ventral thoracic, mediastinal and bronchial lymph centers; (e) lymph nodes of abdomen, including lumbar, coeliac, and cranial mesenteric and caudal mesenteric lymph centers; and (f) lymph nodes of pelvic regin and hind limb, including iliosacral, iliofemoral, inguinofemoral, ischiatic, and popliteal lymph centres (Smuts and Bezuidenhout, 1987).

Histology of lymph nodes:

Stroma

The nodes are encapsulated oval lymphoid structures designated to filter lymph that originates in the interstitial spaces of most of the body's tissues. Each lymph node has afferent vessels penetrating the convex capsular surface and is drained by an efferent lymph vessel emerging from a depression (hilum) along with blood vessels (Samuelson, 2007). Traditionally, histology of lymph nodes could be described as having three compartments: (a) cortex, (b) paracortex, and (c) medulla (Willard-Mack, 2006; Jalkanen and Salmi, 2020). Outside the lymph nodes is a collagenous capsule from which fibrous connective tissue trabeculae extends and divides the subcapsular area into several cortical compartments (lobules). These trabeculae branch and anastomose at the medulla. A network of reticular fibres supports the cellular parenchyma of the lymph node (Willard-Mack, 2006; Jalkanen and Salmi, 2020).

With regard to stroma of the lymph node, there have been various descriptions of the capsule in dromedary lymph node. Zidan and Pabst (2012) mentioned that the capsule is formed of two layers; an outer thicker layer of connective tissue and an inner thinner layer of mainly smooth muscles. Abdel-Magied *et al* (2001) mentioned that the presence of smooth muscle in the capsule was not detected in all examined animals. Later publications mentioned that the nodular capsule is formed of a single layer which is made up of dense, fibrous connective tissue with collagen, a small amount of elastic and reticular fibres, and smooth muscle cells (Gavrylin *et al,* 2013; Rahmoun *et al,* 2020). In sheep and goats, however, no smooth muscle layer was described, and the capsule was formed of fibroelastic connective tissue composed of collagen, elastic and reticular fibres (Senthilkumar *et al,* 2019). While in the cattle, lymph node capsule composed of connective tissue with interspersed smooth muscle cells from which thin trabeculae extended into the cortex (Casteleyn *et al,* 2008b).

From the capsule, the trabeculae extend toward center of the lymph node, dividing parenchyma characteristically into incomplete lobules (Soliman and Mazher, 2005; Zidan and Pabst, 2012). In this respect, two types of trabeculae have been mentioned in dromedary camel: (a) Type I, formed of two layers of connective tissue and muscle in which branches of blood and lymphatic vessels are located, and (b) Type II, formed of smooth muscles only (Garvilin *et al,* 2017).

In the dromedary camel, the lymph node receives one or two large afferent lymphatics that penetrate the capsule. In some camels, these may extend to the connective tissue trabeculae and be drained by 4 or 5 efferent lymphatics (Abdel-Magied *et al,* 2001; Gavrylin *et al,* 2013).

Parenchyma:

The conventional description of parenchyma of the dromedary camel's lymph node as being composed of an outer cortex and inner medulla is not applicable to lymph nodes of other farm animals (Samuelson, 2007). The parenchyma in dromedary camel is composed of lymph nodules that are regularly distributed in the parenchyma, and in between them is a nodular, dense lymphoid tissue and diffuse lymphoid tissue (Fig 9) (Abdel-Magied *et al,* 2001; Soliman and Mazher, 2005; Zidan and Pabst, 2012; Garvilin *et al,* 2017; Rahmoun *et al,* 2020). The parenchyma of lymph node in Bactrian camel is composed of lymphatic nodules, dense anodular lymphoid tissue and diffuse lymphoid tissues (Ye *et al,* 2014; Gahlot *et al,* 2016).

Spleen

Among lymphatic organs of domestic animals, spleen is the largest (Zidan *et al,* 2000a; Samuelson, 2007). In the dromedary camel, it is crescent-shaped and is located at the dorsocaudal aspect of rumen

and extend to the greater omentum (Smuts and Bezuidenhout, 1987; Mohamed, 2020). The spleen is supplied by splenic artery that arises from the coeliac trunk and penetrate spleen at different points of the dorsal end to the middle of the caudal margin (Nawal and Maher, 2018). The splenic artery then branched into cranial and caudal branches in most of the cases, however, middle branch is not uncommon (Radmehr, 1997).

The spleen is surrounded by a thick connective tissue capsule covered externally by mesothelial cells (Alshammary, 2010). The capsule could be easily subdivided into outer and inner layers; the outer layer was composed of connective tissue, including collagen, elastic fibres, and fibroblasts in addition to a few smooth muscle cells whereas, the inner layer was composed mainly of smooth muscles supported by connective tissues (Alshammary, 2010; Maina *et al,* 2014). The trabeculae, either vascular or avascular, extended from capsule to the parenchyma. The vascular trabeculae contained nerve fibres and arteries without veins, but the avascular trabecvlene could be further subdivided into primary and secondary trabeculae. The primary trabeculae were composed mainly of smooth muscle cells supported by reticular, collagen, and elastic fibres (Zidan *et al,* 2000b; Maina *et al,* 2014). The secondary trabeculae were formed of smooth muscle cells with reticular fibres among them (Zidan *et al,* 2000b).

As with other domestic species, the parenchyma of spleen in the dromedary camel is formed of white and red pulps. The white pulp is formed of periarterial lymphatic sheath (PALS) and lymphoid nodules (Zidan *et al,* 2000b). The lymphoid nodules are spherical and sometimes indented on one side. These nodules consist mainly of B-lymphocytes; hence, they represent the B-dependent zone in the spleen (Zidan *et al,* 2000b; Maina *et al,* 2014). The PALS contains 3 to 4 arteries surrounded with T-lymphocytes and is therefore, considered as the T-dependent zone (Zidan *et al,* 2000b).

The red pulp represented by subcapsular blood sinuses which are connected to the peritrabecular sinuses. Furthermore, the red pulp is divided by secondary trabeculae resulting into smaller compartments, the splenic cords. Each cord formed of a reticular network that contains different blood cells (Zidan *at el,* 2000b).

To the best of the author knowledge, no morphological and histological study has been performed on the spleen of the Bactrian camel. In the previous literature, domestic ruminants have similar structural components, in terms of spleen stroma and parenchyma, as that of the dromedary camel (Samuelson, 2007; Suri *et al,* 2017; Gnanadevi *et al,* 2019).

Haemal Nodes

Haemal nodes are encapsulated haematopoietic and lymphoid organs that have been reported in some mammals such as humans, rats and ruminants (Zhang *et al,* 2012b). They were described as spleen-like structures located retroperitoneally along the vertebral column (Banks, 1993). In camels, the hemal nodes are brown to dark-red and are spherical or kidney-shaped embedded in the fat of the abdominal and pelvic cavities. Their size varied from 2 to 12 mm in diameter (Zidan and Pabst, 2004). However, Hussin (2016) described their shape as conical with convex base and apex. Histologically, each node consisted of a capsule enclosing the parenchyma. They may have more than one hilum where arteries and nerves enter and veins and lymphatics leave the node. The parenchyma of the haemal node is composed of a cortex and a medulla supported by reticular fibres. The cortex is formed of lymphoid nodules and diffuse internodular lymphocytes (Zidan and Pabst, 2004; Hussin, 2016). Interestingly, Zidan and Pabst (2002) detected several apoptotic cells within the germinal centers of the lymphoid nodules.

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