Histopathological Study of the Lymphoid Organs in Different Species of Egyptian Rats

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Abstract: The development of lymphoid organs depends on the correct expression of several molecules within a defined timeframe during ontogeny. Although this is an extremely complex process, with each secondary lymphoid tissue requiring subtly different signals, a common framework for lymphoid development is beginning to emerge. So, we selected three species of the most common Egyptian rats, *Arvicanthis niloticus*, *Microtus agrestis* and *Acomys cahirinus* to determine whether or not there are interspecific differences in their lymph nodes. The possibility of interspecific differences is important because the selected species represent three significantly different size categories (small, represented by *M. agrestis*, moderate represented by *A. cahirinus*, and large represented by *A. niloticus*) with presumably different diets and different physiologic strategies. Also, the random variations of the lymph node number within species of *A. niloticus*, *M. agrestis* and *A. cahirinus* were noted. These individual variations are remarkable in the posterior cervical, brachial, internal jugular and axillary lymph groups.
[Abdel-Hakim Saad, Rewaida A. Abdel-Gaber, and Hanaa M. Mahmoud. **Histopathological Study of the Lymphoid Organs in Different Species of Egyptian Rats.** *J Am Sci* 2013;9(3):93-105]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 13

Keywords: Arvicanthis niloticus - Microtus agrestis - Acomys cahirinus - Lymphocyte

1. Introduction

The lymphatic system occupies a very important position in physiology, pathology and clinical medicine, as is attested by its relation to tissue drainage, digestion, infection and inflammation, malignancy and edema. However, the increase in knowledge along this line depends considerably on the development of data concerning the anatomy and distribution of the entire system (Higgins 1925). Nopajaroonsri *et al*. (1971) considered the lymph nodes as highly specialized immune-competent organs with distinct cellular characteristics which are altered in a specific manner in response to different forms of antigenic stimulation. Lymph nodes of some rodent species have been extensively studied by light and electron microscopy and their histological features are well known (Job 1922; Dawson and Masur 1929; Fischer 1939; Han 1961; Clark 1962; Trurner 1969, 1971; Nopajaroonari *et al*. 1971; Macmillan *et al*. 1974; Jia *et al*. 2012). Previous investigations (Job, 1915; Greene, 1935; Sanders and Florey, 1940) have concentrated primarily upon the location of the lymphoid tissue. Indeed, Miotti (1961, 1965) stressed visceral drainage of golden hamster and *Rattus norvegicus*; while Higgins (1925) has described only the lymphatic system of the newborn rat. An extensive definition of both somatic and visceral lymphatic routes was presented by Tilney (1971). However, there was no comparative study concerned different rodent species.

As the rodents are the most abundant and taxonomically difficult mammals, as the Myomorphs are the most common of rodents. They are represented by three fairly distinctive groups; the Muroidea; which are treated in this study and are the nucleus of the suborder Gliroidea and Dipodoidea (Simpson 1945). The essential members of the Muroidea group are Cricetidae and Muridae. Many authorities do not recognize the Circetidae and Muridae as separate or natural families (Thomas 1897; Ellerman 1941; Hooper and Musser 1964; Roberts 1970; Mascarello *et al*. 1974; Pocock 1976; Osborn and Helmy 1980). There is seem, however, to be little serious doubt, that they are natural units (Li *et al*. 2012).

The present study was undertaken to assess the distribution and morphology of the structure of lymph node groups from three species of rats: *Arvicanthis niloticus*, *Microtus agrestis* and *Acomys cahirinus*. Rats were used in favor of mice because of their larger size, which facilitates the identification of lymphoid nodules. Besides the intrinsic scientific interest in normal structure and function of the immune system of rats, a practical need for the knowledge of these structures arose recently. From an evolutionary point of view, no specific structural adaptations have been found in respect of the lymph nodes of the three species tested. The entire lymph nodes anatomy, distribution and morphological structure fall entirely into the general mammalian pattern (Fu and Chaolin 1999; Patriara *et al*. 1994; Mebius 2003; Suzuki *et al*. 2008).

2. Materials and Methods

All studies and experimented procedures followed the guiding principles in guide for the care and use of laboratory animal and were approved by the Institutional Animal Care and use Committee of Cairo University, Cairo, Egypt.

Animals: Three species of rats from two different families were used in the present study. One previously studied species, *Rattus norvegicus* have been investigated at first as control model.

Family: Arvicollidae

Genus: Clethrionomus: *Micortus agrestis* (Linnaeus 1761)

Family: Muridae

Genus: Arvicanthis: *Arvicanthis niloticus* (Desmarest 1822)

Genus: Acomys: *Acomys cahirinus* (Desmarest 1891)

Genus: Rattus: *Rattus norvegicus* **(**Berkenhout 1769)

Morphology of the lymph nodes

At least 10 specimens from each species were killed by ether overdose and dissected directly within few minutes. By the aid of binoculars, regional lymph nodes were examined in all mentioned species. Sketches with the location of the nodes were prepared indicating location, relative size and number of lymph nodes on both sides of the body. A general model of the animal features was drawn and repeated for the different aspects with the delineation of their characteristic lymph node distribution. The nomenclature of lymph nodes is according to **Job (1922), Sanders and Florey (1940) and Zahran (1986).** The specimen of the adult laboratory rat (*Rattus norvegicus*) was investigated as control model of the lymph node distribution.

Histology of the lymph nodes

Light microscopical study:

The present study concentrated on some lymph nodes of appreciable size because the other lymph nodes where embedded in the surrounding tissues which make them difficult to be prepared for routine histological analysis. The rats were killed, dissected and the investigated lymph nodes were removed and immediately placed in Bouin's fixative. Then, the tissues were dehydrated, embedded in Paraffin, sectioned at 5 µm and stained with hematoxylin-eosin.

Electron microscopical study:

Lymph nodes were removed, and fixed by immersion in 2.5% glutaraldehyde buffered to pH 7.2 with Millonig's fluid. The tissues were then post-fixed in 1% OsO4 in the same buffer and dehydrated in acetone for embedding in Araldite. Ultrathin sections were obtained with a Reichert OM-43 Ultratome; then doubly- stained with lead citrate and uranyl acetate, and examined in Joel 100 C electron microscope. Semi-thin sections; approximately 1-2 µm in thickness; were stained with alkaline toluidine blue for selecting the most adequate areas.

3. Results

Histological structures of lymph nodes

Arvicanthis niloticus

The superficial cervical lymph nodes:

The capsule which was slightly thick, showed lymphocytic infiltration, and invaded in some places by plasma cells. The cortex showed well-defined nodules, which were located at the periphery of the node. Few of them are circular or crescent peripheral zones of deeply stained lymphocytes (Fig. 1A). The medulla which occupied a large part of the node contained ill-defined nodules had germinal centers. The latter was characterized by the presence of medullary cords with medullary sinuses. The peripheral sinuses (subcapsular sinuses) which separated the nodes from the capsule were very narrow and lacked in some areas of the nodes (Fig. 1B).

The Inguinal lymph nodes:

The capsule was greatly thicker than that of superficial cervical lymph nodes and was invaded with a large number of lymphocytes (Fig. 2A). The cortex of some nodes contained few nodules, while others showed no nodules or evidences of differentiated cortex. The nodules, when present, lacked germinal centers. However, they exhibited a large number of lymphocytes, plasma cells and pigment-containing macrophages. The medulla showed ill-defined medullary cords, with medullary sinuses (Fig. 2B).

The axillary lymph nodes:

The capsule which was slightly thick was invaded by lymphocytes and in some places by plasma cells (Fig. 3A). The cortex occupied most of the nodes, and contained several nodules with prominent germinal centers. The nodules exhibited a large number of lymphocytes, plasma cells and pigment-containing macrophages. The medulla was reduced in size and had well-defined medullary cords and narrow medullary sinuses. The peripheral sinuses were relatively wide; while the medullary sinuses were narrow (Fig. 3B).

The superficial mesenteric lymph nodes:

The capsule was thick and invaded with lymphocytes and plasma cells (Fig. 4A). The cortex occupied most of the node and consisted of numerous nodules, with prominent germinal centers. Numerous pigment-containing macrophages and plasma cells were, detected in these nodules (Fig. 4B). The medulla showed ill-defined medullary

cords. The subcapsular sinuses contained numerous lymphocytes and macrophages.

Microtus agrestis

The superficial cervical lymph nodes:

The nodular cortex appeared to accommodate high level of small lymphocytes (Fig. 5A). Discrete follicles might be observed in the inner part of the cortex. The diffuse cortex contained a large number of small lymphocytes that were not arranged as follicles. Medium-sized lymphocytes were not frequently seen in the cortex of lymph nodes (Fig. 5A). Only minimal changes could be detected in the small lymphocytes of the diffuse cortex. No primary follicles were seen even in areas that appeared to be mildly depleted of lymphocytes. The inner cortex was found to be depleted of small lymphocytes. The outer cortex appeared to accommodate the relatively small number of lymphocytes (Figs. 5A,B).

The axillary and gluteal lymph nodes:

It showed a clear demarcation between the peripheral cortex, paracortex and medulla (Figs. 6A,B). In contrast, small gluteal lymph nodes with indistinct compartmentalization and decrease cellularity were observed (Fig. 6C). Compared to *A. niloticus*, neither cortical expansion nor capsular indentations were detected in the lymph nodes. In contrast to the nodular cortex which was severely affected, only minimal changes could be detected in small lymphocytes of the diffuse cortex (Fig. 6D).

The superior mesenteric lymph nodes:

The cortex was divided into two zones: the nodular and the diffuse cortex (Fig. 7A). The nodular cortex consisted of a variable number of densely packed small lymphocytes, forming primary follicles, and was observed mainly in the outer part just next to the capsule (Fig. 7A). The outer cortex was expanded by lymphocytic aggregations. Discrete follicles were only observed in the inner cortex. The diffuse cortex contained a large number of small lymphocytes that were not arranged into follicles (Fig. 7B). They were located between the first zone and the medulla, and partially between follicles of the outer part of the cortex. Medium-sized lymphocytes were not frequently seen in the cortex of lymph nodes (Fig. 7A,B).

The inferior mesenteric lymph nodes:

The inner cortex was found to be depleted of small lymphocytes (Fig. 7C). No primary follicles were seen even in areas that appeared to be only mildly depleted of lymphocytes (Fig. 7C). The outer cortex appeared to be housed by relatively small number of lymphocytes. Numerous pyknotic lymphocytes could be observed in the medulla (Fig. 7D).

The brachial and internal jugular lymph node:

It showed a clear demarcation between the peripheral cortex, paracortex and medulla (Figs. 8A,B). The outer cortex contained relatively small lymphocytes (Fig. 8A). The diffuse cortex contained a discrete number of lymphocyte aggregations that were arranged as follicles (Fig. 8B). The internal jugular lymph nodes showed an intense disorganization of the lymphoid tissues with hypocellularity of cortical nodules and medullary cords, loss of germinal center (Fig. 8C), and numerous pyknotic lymphocytes (Fig. 8D).

The renal lymph nodes:

They were encapsulated by a thin fibrous capsule with no lymphocytic infiltration (Fig. 9A). The cortex occupied a small space of the nodes and contained very darkly stained nodules and to some extent lacked germinal centers (Fig. 9B). The medulla which occupied a large part of the node contained ill-defined medullary cords with medullary sinuses (Fig. 9B).

Acomys cahirinus

The brachial lymph nodes:

The covering capsule was generally thicker than that of other lymph nodes and invaded by lymphocytes and plasma cells (Fig. 10A). The cortex occupied a small space of the node and showed well-defined nodules located at the periphery of the node (Fig. 10B). They exhibited prominent germinal centers with lymphocytes and plasma cells. The medulla showed ill-defined medullary cords. The subcapsular sinuses were very narrow and were lacked in some areas of the node (Fig. 10C).

The inferior mesenteric lymph nodes:

The number of plasma cells increased markedly and plasma cells are seen singly or in small groups in the paracortex (Fig. 11A). They appeared to accumulate in the medullary cord, especially close to the paracortex. They are sometimes distributed throughout the medulla. In some animals, the medullary cords become enlarged and filled with plasma cells (Fig. 11B). Plasma cells showed occasional mitotic figures and the medullary sinuses appeared compressed and narrowed. After that, they accumulated not only in the medullary cord, but also in the paracortex.

The internal jugular lymph nodes:

The medullary cords (Fig. 12B) are markedly enlarged with large accumulation of plasma cells, when compared with those of the cortex (Fig. 12A). On the cortex (Fig. 12A) and paracortex, however, plasma cells are rarely seen (Figs. 12A,B).

Other lymph nodes:

Axillary (Figs. 13A and B) and gluteal (Figs. 13C) lymph nodes are histologically similar in appearance in *A. cahirinus*. In the medulla, the

frequency of plasma cells does not show any significant changes (Fig. 13B).

Ultrastructure study of lymph nodes

The cortex: In the cortex of the superficial cervical lymph node of *A. niloticus*, two regions can be clearly distinguished; the areas where the follicles are located (Fig. 14A) and the paracortical zone between the follicles which is continuous with the medullary region (Fig. 14B). The vast majority of the follicles in the brachial lymph nodes are secondary clearly delineated germinal centers, which are surrounded by a darker stained mantle zone. It contains tightly packed monomorphic intensely stained small lymphocytes (Fig. 14C). The mantle zone in the brachial lymph nodes forms a thick cap on the side where the follicles face the sinus (Fig. 14D). Small lymphocytes can be in the found in the cortical region of the gluteal lymph nodes (Fig. 14D).

The germinal center up the superficial cervical lymph nodes of *M. agrestis* can be divided into two parts. First is lighter stain zone consisting predominately of centrocites, which can be recognized by their oval cytoplasm and their cleaved nucleus (Fig. 20A). The second zone is stained darker and consists of centroblasts, which can be recognized by their basophilic cytoplasm, and their large nucleus containing several marginally located nucleoli (Fig. 15A). Macrophages with heteromorphy lysosomes and multinucleated giant cells with smooth rimmed chromatin-rich nuclei are occasionally found in the gluteal lymph nodes (Fig. 14B). Dendritic reticulum cells are in the superior mesenteric lymph nodes characterized by a cleaved nucleus with a fine granular, electron-dense heterochromatin and a centrally located nucleolus (Fig. 20C). Numerous small lymphocytes can be found adjacent to these cells. In addition, larger lymphocytes, centroblasts, with a pale nucleus and large nucleolus, large rim of cytoplasm with mitochondria, ribosome and cisternae of RER can be found in the brachial and internal jugular lymph nodes. These cells are tightly packed in groups with close apposition of the neighboring cell membranes. The whole cortical region mainly the paracortical region of the renal lymph nodes is rich in blood vessels, particularly veins. The endothelia rest on a well-developed basal lamina which is covered by collagen fibrils (Fig. 14D).

In the cortex of the brachial lymph nodes in *A. cahirinus*, follicles are clearly distinguished and surrounded by a darker stained zone (Fig. 15A). Mitotic figures can be seen. Numerous lymphocytes can be seen adjacent to the dark zone of the inferior mesenteric lymph nodes (Fig. 15B). The larger lymphocytes found adjacent to the dark zone in the internal jugular lymph nodes recognized by their basophilic cytoplasm and large nucleus and large rim of cytoplasm (Fig 15C). Numerous small lymphocytes and macrophages with lysosomes and multinucleated giant cells with a pale nucleus and large nucleolus can be found in the gluteal lymph nodes (Fig. 15D).

The paracortex:

The paracortex area stretches from the region between the follicles into the medullary part of different lymph nodes (Fig. 16A,B) and is characterized by small-medium monomorphic lymphocytes tightly packed into small groups which are often oriented in radial strands towards the medullary sinus. The lymphocytes in the lymph nodes of *M. agrestis* are morphologically uniform with a moderate density of the heterochromatin in the nucleus, often containing several nucleoli (Figs. 17A,B). Due to the uniform morphology of the lymphocytes, no further morphological subdivision of the lymphocyte population in the lymph nodes of *A. cahirinus* is possible. Inter-digitating reticulum cells are rarely found in the different lymph nodes.

The medulla:

Medullary cords of the lymph nodes of *A. niloticus* separated by the medullary sinuses, which have broad lumina and are built up by a loose meshwork of reticulum fibers filled with lymphocytes and plasma cells, are the distinguishing features of the medullary zone of the lymph nodes (Figs. 18A,B).

The extracellular matrix of the lymph nodes of *M. agerstis* is made up of collagen fibrils which are either oriented in parallel fibrils or in a felt work like fashion (Figs. 19A,B). Plasma cells are common, often grouped together, and are characterized by their round to oval, eccentrically located nucleus with the typical cartwheel pattern of heterochromatin distribution (Fig. 19A). The large cytoplasm is filled with a partly dilated RER. In the whole medullary region, fibroblastic reticulum cells are found only occasionally (Fig. 19B). Mast cells are common in the medullary region of the lymph nodes of *A. cahirinus* and are often group together or in conjunction with plasma cells (Figs. 20A,B). The cytoplasm of the mast cells is characterized by the presence of numerous round granules containing coarse particles of meandering filamentous structures (Figs. 20A,B).

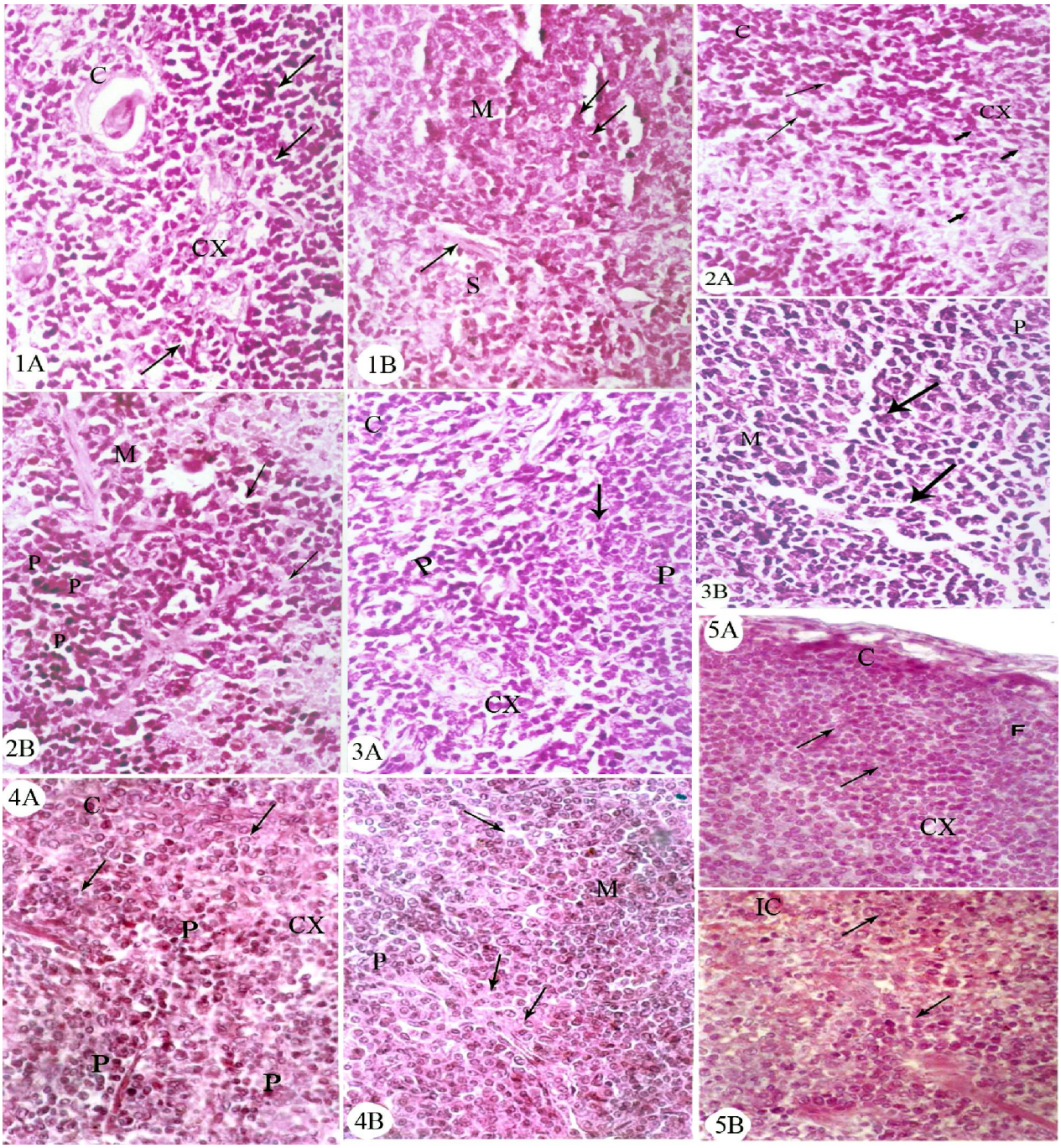

Fig. 1A,B: The superficial cervical lymph node of *A. niloticus*. Arrows indicate the position of germinal centers. **Fig. 2A,B:** The inguinal lymph node of *A. niloticus*. Arrows indicate aggregation of lymphocytes. Arrow head indicate plasma cells. **Fig. 3A,B:** The axillary lymph node of *A. niloticus*. Arrows indicate germinal centers. Fig. 4A,B: The superior mesentric lymph node of *A. niloticus*. Arrows indicate germinal center arrow heads indicate pigment-containing. Fig. 5A,B: The superficial cervical lymph node of *Microtus agrestis*. Arrows indicate the portion of diffuse follicles in the cortex. C: Capsule; CX: Cortex; M: Medulla; S: Subcapsular cortex; P: Pigment; F: Follicles; IC: Inner cortex. X 100

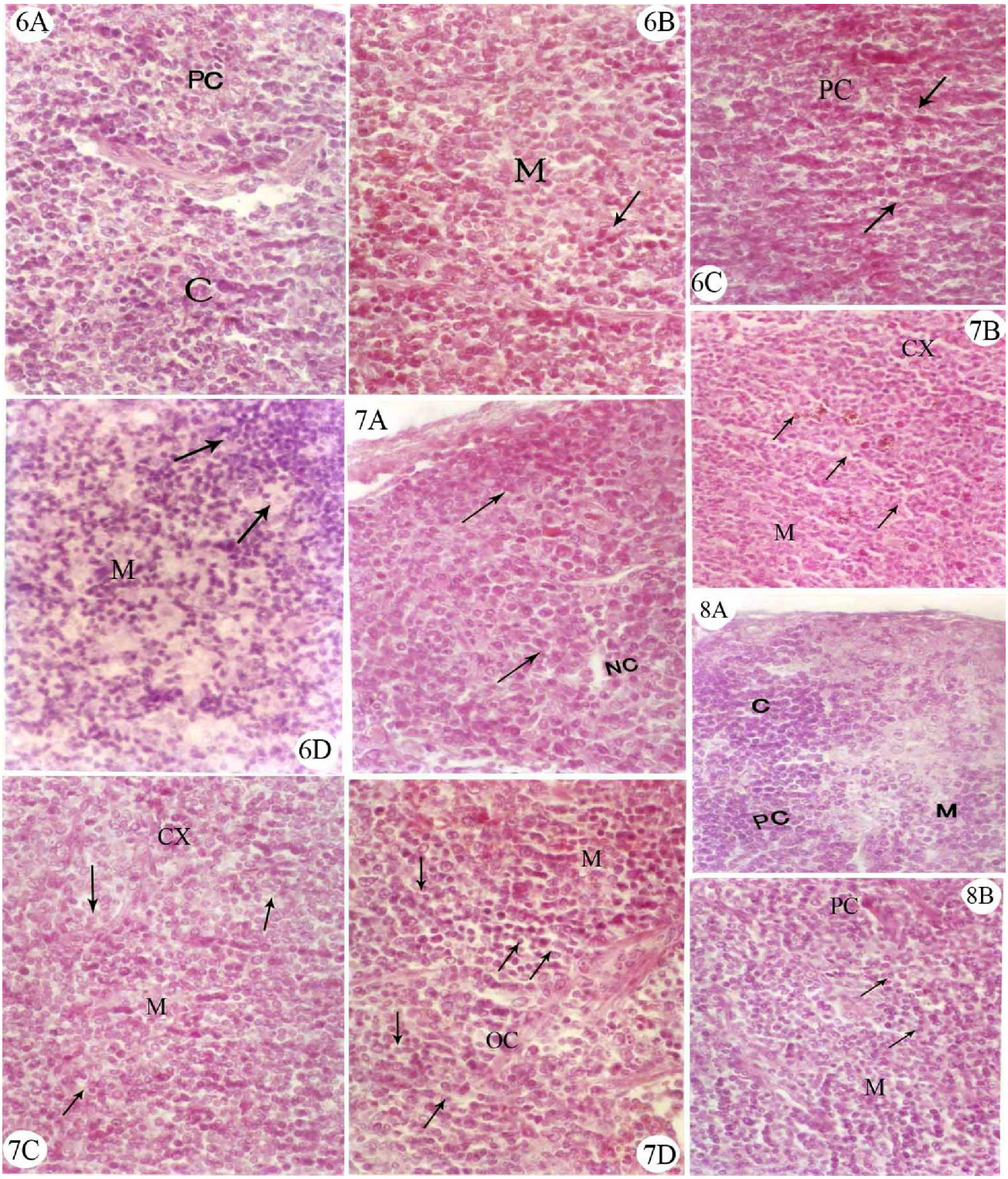

Fig. 6: The axillary (A,B) and the gluteal (C, D) lymph nodes of *M. agrestis*. Arrows indicate the portion of small lymphocytes. Fig. 7: The superior (A,B) and inferior (C,D) mesenteric lymph nodes of *M. agrestis*. Arrows indicate position of pyknotic lymphocytes. Fig. 8A,B: The brachial lymph node of *M. agrestis*. Arrows indicate lymphocyte aggregations. C: Capsule; PC: Paracortex; M: Medulla; NC: Nodullar cortex; CX: Cortex; OC: Outer cortex. X 100

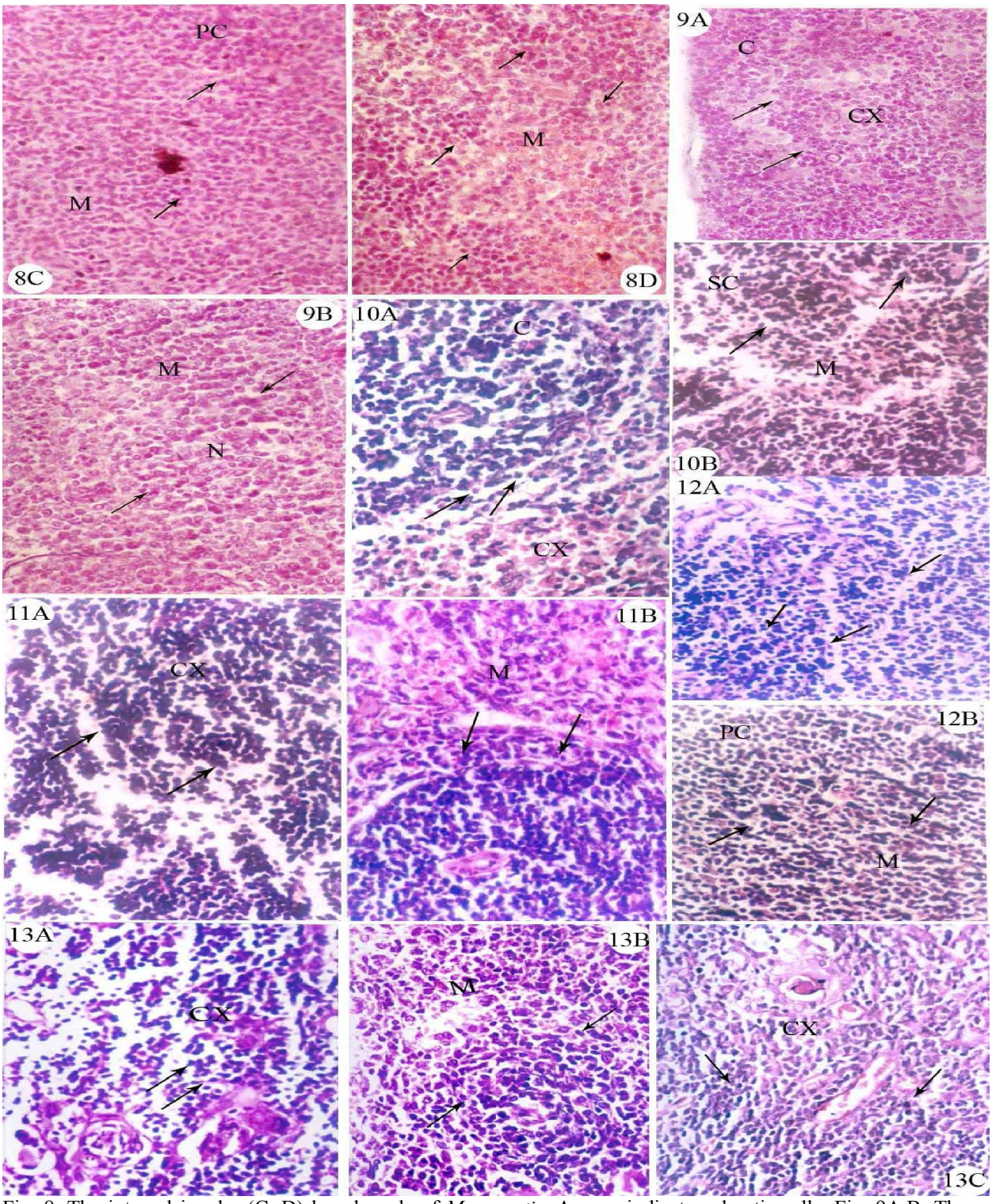

Fig. 8: The internal jugular (C, D) lymph node of *M. agrestis*. Arrows indicate pyknotic cells. Fig. 9A,B: The renal lymph nodes of *M. agrestis*. Arrows indicate medullary sinuses. Fig. 10A,B: The brachial lymph node of *Acomys cahirinus*. Arrows indicate lymphoid nodules. Fig. 11A,B: The inferior mesenteric lymph node of *A. cahirinus*. Arrows indicate the position of plasma cells. Fig. 12A,B: The internal jugular lymph node of *A. cahirinus*. Arrows indicate accumulation of plasma cells. Fig. 13: The axillary (A,B) and gluteal (C) lymph nodes of *A. cahirinus*. Arrows indicate the position of plasma cells. C: Capsule; PC: Paracortex; M: Medulla; CX: Cortex; N: Nodule; SC: Subcapsular sinus. X 100

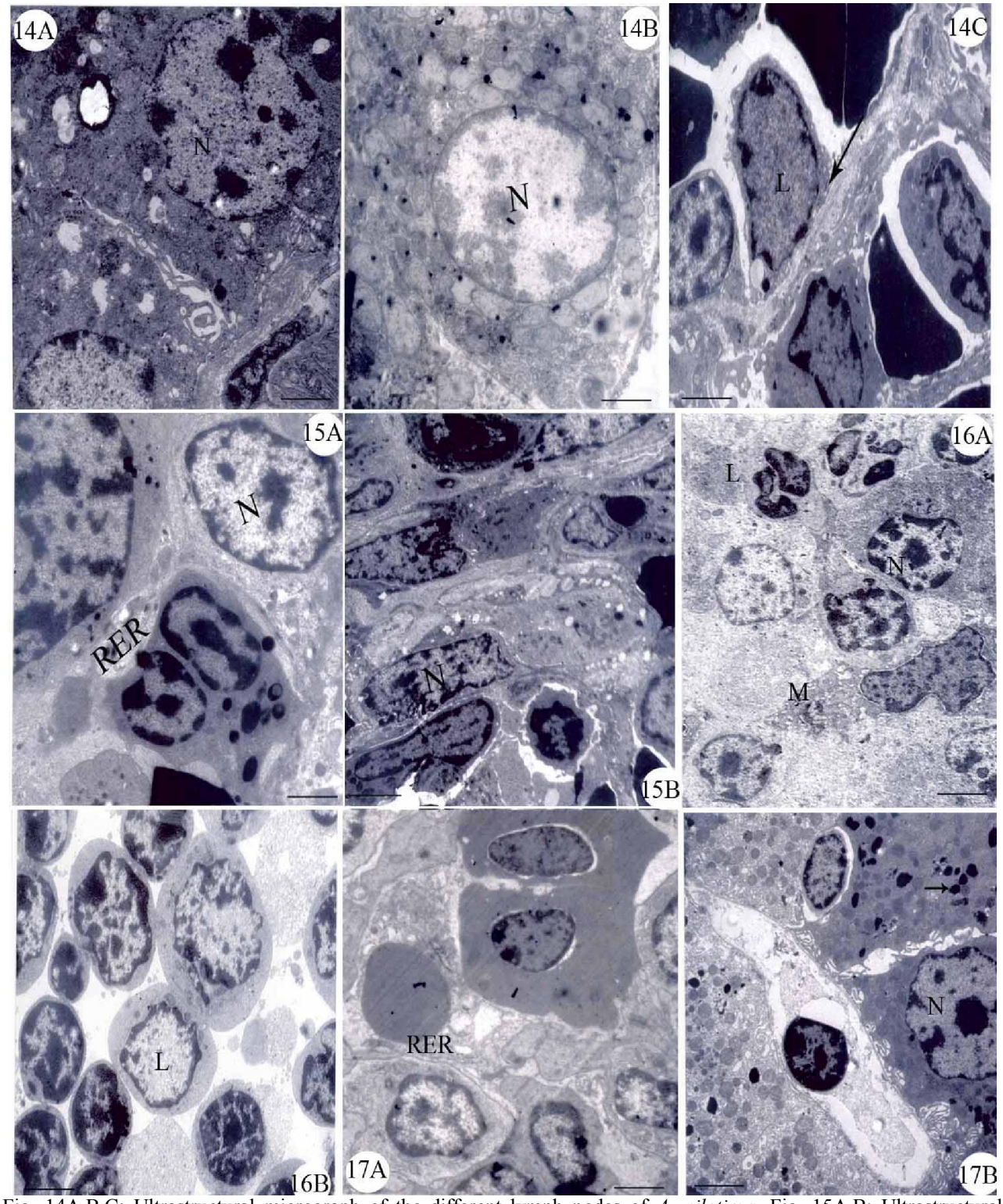

Fig. 14A,B,C: Ultrastructural micrograph of the different lymph nodes of *A. niloticus*. Fig. 15A,B: Ultrastructural micrograph of the different lymph nodes of *M. agrestis*. Fig. 16A,B: Ultrastructural micrograph of the different lymph nodes of *A. cahirinus*. Fig. 17A,B: Ultrastructural micrograph of the different lymph nodes of *A. niloticus*. Arrow indicate pigment granule. N: Nucleus; l: Lymphocyte; M: Mitochondria; RER: Rough endoplasmic reticulum. X 20.000

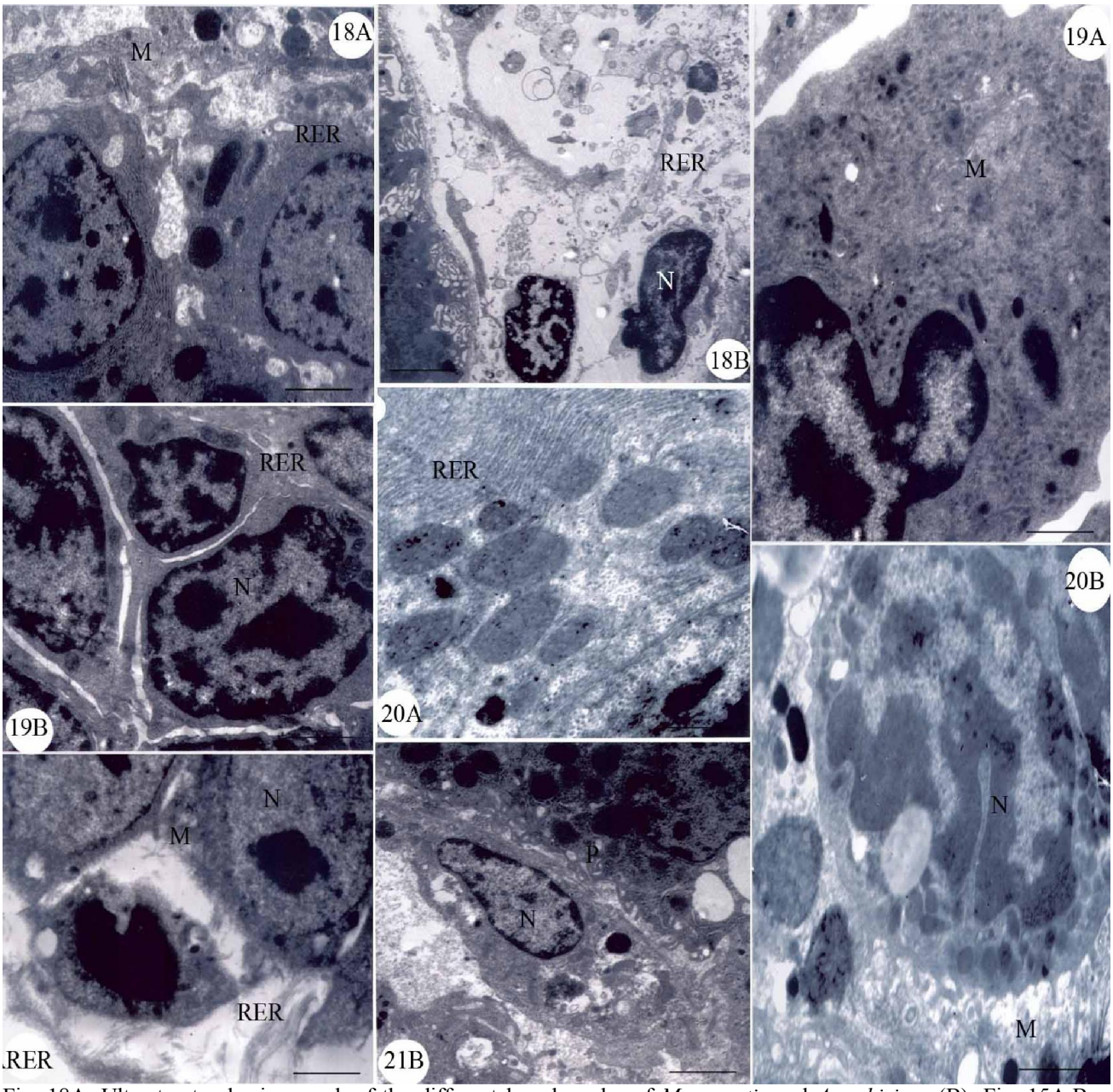

Fig. 18A: Ultrastructural micrograph of the different lymph nodes of *M. agrestis* and *A. cahirinus* (B). Fig. 15A,B: Ultrastructural micrograph of the different lymph nodes of *M. agrestis*. Fig. 19A,B: Ultrastructural micrograph of the different lymph nodes of *A. niloticus*. Fig. 20A,B: Ultrastructural micrograph of the different lymph nodes of *M. agrestis*. Fig. 21A,B: Ultrastructural micrograph of the different lymph nodes of *A. cahirinus*. N: Nucleus; M: Mitochondria; RER: Rough endoplasmic reticulum; P: Pigment. X 20.000

4. Discussion

From the data obtained from this study, it seems evident that there is a definite plan in the structure and arrangement of the lymph nodes in species with a wide degree of variation in number of nodes (Grau 1974). However, the lymph nodes are few and small in rodents, more numerous in carnivores and better developed in man than in other forms (Gulland 1894). From the foregoing it is evident that the lymph nodes of herbivorous species have a generally better developed lymphoid tissue in the form of lymph nodes than that of insectivorous species. The occurrence of the superior mesenteric lymph nodes, but total absence of inferior mesenteric lymph nodes in *A. niloticus* is also significant. This is suggestive of the possibility that the food of this species may have content of pathogenic bacteria (Pei *et al*. 2001; Suzuki *et al*.

2008). Similarly, the food of *M. agrestis* may be assumed to be of low bacteria content since it feeds on large freshly insects. The occurrence of both posterior and inferior mesenteric lymph nodes in *M. agrestis* at the viscera may be sufficient, to meet the defense demands of this species and ensure bactericidal action at one place only (Pei *et al*. 2001; Suzuki *et al*. 2008; Li *et al*. 2012; Jia *et al*. 2012).

Instability of the lymph node number even in normal animals, has been demonstrated in albino rat (Kindred 1938; Tilney 1971), laboratory rat (Tilney 1971), guinea pig (MacMillan 1974), and gerbil (Zahran 1986). The changes occurring within the lymph nodes are believed to result largely from the dis-function of the normal lymphocytic drainages (Kindred, 1938). Also, in the present study, there is no correlation in size between nodes from the same animal. The thoracic and mesenteric groups in the different investigated specimens may vary in number, due to the fact that several lymph nodes frequently fuse together to form continuous lymphoid aggregations. The mesenteric lymph nodes represent the most variable group in the body. This variability may be attributed to the constant chance of infections through the digestive tract. In addition, some lymph nodes grouped and lobulated, such as the facial, inguinal and mesenteric nodes in both *R. norvegicus* and *A. niloticus* (Tilney 1971; Zahran 1986). For instance, the absence of the iliac lymph nodes in *M. agrestis* and *A. cahirinus* is accompanied by the presence of the gluteal node. Both groups of lymph nodes drain the same parts of the body and have the same afferent drainage to the renal nodes. The approximate total absence of the inguinal group in *M. agrestis* and *A. cahirinus* which drain the gluteal area and lateral aspect of the tail (Tilney 1971), is substituted by the presence of the gluteal nodes due to the fact that specimens are characterized by their short tail. However, this suggestion is not valid for *A. cahirinus* which has a long tail. Also, the inferior mesenteric group is only present in *M. agrestis* and *A. cahirinus* and not observed in *A. niloticus*. This group of lymph node has the same function as the superior mesenteric group. However, the number of other groups of lymph nodes in *A. cahirinus* is small in comparison with other investigated species; the maximum number of them is two, but they are of larger size. Moreover, the appearance of certain lymph nodes in individual of the same species may be related to the occasional need of the body to these nodes as has been suggested earlier (Job 1922; Andrew and Andrew 1948; Bloom and Fawcett 1968). This feature is supported by fluctuation in presence of the posterior cervical nodes, which have the same function as the internal jugular nodes. They are lying close to each other's and were recorded in most of the studied individuals. However, the observation of the popliteal and inguinal groups only in *A. niloticus* may confirm this fact.

Lymph nodes of rats, in general, are encapsulated by a thick layer of fibrous connective tissue with subcapsular sinuses underneath. The capsule is thicker at hilus, where ingoing and outgoing vascular channels are located. The demarcation of cortex and medulla are more prominent than in mice. Primary lymphoid nodules are present in the cortex. Cortex is demarcated into outer and inner cortex (Job 1922; Han 1961; Gulland 1984; Fu and Chaolin 1999; Mebius 2003; Suzuki *et al*. 2008). In the present study, random distribution of lymphocytes in the sinuses of the examined nodes and also the invasion of the node capsule with lymphocytes was clearly demonstrated especially in the axillary and posterior cervical nodes. The detection of the germinal centers in the cortical nodules of the axillary and gluteal nodes and the lacking of these centers in the other nodes such as the posterior cervical, brachial and renal nodes depends on the demands for immunological function. According to Ham (1974), lymph nodes constitute one line of defense against diseases, since they are the site of production of the lymphocytes, and they contain phagocytic cells that can ingest and destroy bacteria, virus as well as foreign particles and cellular debris. In this respect, they serve as filtering beds for interstitial fluid before the latter is returned to the general circulation. Moreover, the predominance of the cortex over the medulla in the posterior cervical, axillary and gluteal nodes was characterized by the increase of their lymphocyte population. The variations in the boundaries between the cortex and medulla as demonstrated in the posterior cervical, axillary and gluteal nodes might reflect variations in the importance of the immunological reactions undergone by the cortical part. This phenomenon was postulated in different animal models (Belisle and Sainte Marie 1981; Mills 1989; Zahran 1986).

The principal subdivision of the cortex and the paracortical region as seen in other mammals can also be observed in the tested species. Most of the follicles appear as germinal centers which are indicative of an active humoral immune response since the priming and maturation of B-cells takes place in this area (Marco *et al*. 1992). The presence of an active immune response in the superior mesenteric lymph nodes of *A. niloticus* and *M. agrestis* which directly drain the paracortical lymph nodes is in accordance with quantitative immune-histochemical data from mammalian lymph nodes, indicating that paracortical lymph nodes are

immunologically more active than axillary lymph nodes (Higgins and Garham 1929; Olin and Saldeen 1946; Courtice and Steinback 1950; Marco *et al*. 1992). As typical for lymphoid follicles in other species including man (Bloom and Fawcett 1968), the lymphocyte wall forms a cap and is thicker on the side directed towards the sinuses. The internal division of the germinal centers into the areas containing centrocytes and those containing centroblasts, both containing dendritic cells as found in other mammals (Ezaki *et al*. 2004), is also observed in lymph nodes of tested species. The similarity of the fine structure of the cortex of lymph node for rats with that of other mammals also extends to the organization of the lymphocytes and the presence of high endothelial venules. Inter-digitating reticulum cells are similar in morphology to those described in humans (Kaiserling and Wolburg 1988; Kaku *et al*. 1997; Windmill and Lee 1998; Naito *et al*. 1999; Li *et al*. 2000; Maruyama *et al*. 2006; Suzuki *et al*. 2008; Li *et al*. 2012; Jia *et al*. 2012).

The last distinguishable region is the medullary region characterized by medullary cords separated by medullary sinuses and the presence of abundant mast cells, often found in small clusters which regarded as a sign of immunological activation in the lymph nodes of man (Lennert and Illert 1959) and other animals (Chiarin-Garcia and Pereira 1999). This interpretation would be in accordance with the high number of germinal centers observed in the cortex of lymph node observed in this study, which is also interpreted as a sign of immunological stimulation. In rodents, the number of mast cells rapidly increases in lymph node draining the site of localized primary antigenic or even non-antigenic stimuli (Miller and Cole 1968; Roberts 1970; Wlodrski *et al*. 1973; Sainte-Marie and Peng 1990; Haynes 1991; Swieter *et al*. 1992; Metcalfe *et al*. 1997). Histamine that is predominantly stored in mast cells is considered to be an important modulator of the immune response (Khan *et al*. 1986). Moreover, several biological effects have been ascribed to heparin, including protective actions against toxic substances, activation of macrophages, a role in leukocyte migration (Miller and Cole 1968) and inhibition of the proliferative responses of T and B lymphocytes (Gorski *et al*. 1991).

The presence of distinct population of mast cells inside the lymph nodes of the tested species showed that, whatever function they have, it may depend on their localization in the nodal tissue. In mammals, some evidences indicate that the medullary sinuses mast cells represent a functional subpopulation: they are neither markedly increased in the athymic state nor markedly decreased in germ-free rats, and so could be primarily related to non-immunological events (Sainte-Marie and Peng 1990). In the tested species of rats, existence of a morphological distinct population of mast cells inside the medullary sinuses in lymph nodes from different anatomical regions reinforces this possibility. Plasma cells are another very common feature of this region, and in experimental studies their number in the medullar region of the lymph nodes increases after antigenic stimulation (Novotny *et al*. 1994), again arguing for the immunological active nature of these lymph nodes.

In summary, we concluded the absence of some lymph nodes in the three investigated species; *A. niloticus*, *M. agrestis* and *A. cahirinus* in comparison with that present in *Rattus norvegicus*. However, the absence of these nodes is substituted by other groups, which drain the same region to meet the defense demands of this species.

Acknowledgment

This work was supported by Faculty of Science, Cairo University, Egypt.

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1/12/2013