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Plasma Cell Proliferation In The Harderian Gland During The Development And Involution Stages of bursa of Fabricius

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Abstract:
Background*: Harderian gland in avian is different from other vertebrates due to the presence of unexpected number of plasma cells in interstitium. In this study, the relation between the increase in the number of plasma in the Harderian gland of chukar Partridge (Alectoris chukar) and bursa of Fabricius development and involution periods was investigated histologically.*
Materials and Methods*: In this study, Harderian glands and bursa of Fabricius of 20 3 month old (10 male, 10 female), 20 6 month old (10 male, 10 female) brown partridges purchased from a commercial farm (Turkey / Antalya) were used.Harderian gland and bursa of Fabricius tissue samples, which were taken as total, were determined by keeping them in 10% neutral formaldehyde for 24 hours. Tissue fragments were blocked in paraffin following the known histological techniques such as washing, dehydration and polishing processes. 5 µm thick sections taken from the blocks were subjected to the following procedures.Harderian gland and bursa of Fabricius tissue samples, which were taken as total, were determined by keeping them in 10% neutral formaldehyde for 24 hours. Tissue fragments were blocked in paraffin following the known histological techniques such as washing, dehydration and polishing processes.*
Results*: According to findings, the relationship between 3 month-old (male/female) Harderian gland and 3 month-old (male/female) bursa of Fabricius plasma cell numbers was statistically significant (p <0.001). The relationship between 6 month-old (male/ female) Harderian gland and 6 month-old (male/female) bursa of Fabricius plasma cell numbers was also statistically significant (p <0.001).*
Conclusion: *Findings from this study strengthen the view that the Harderian gland is an alternative organ to the bursa of Fabricius in the avian.*
Key Word*: Harderian gland; bursa of Fabricius; plasma cell; immunology; avian.*

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I. Introduction

The avian Harderian gland is a peripheral lymphoid organ located at the variable aspect of the orbit of the chicken, and plays an important role in immunological defense of the paraocular region in addition to its primary functions of producing lacrimal fluid, photo protection and acting as a source of pheromones and thermoregulatory lipids, as well as a site of osmoregulation[1,2,3].

Harderian gland in the avian is different from other vertebrates due to the presence of an unexpected number of plasma cells in the interstitium[2,4,5,6,7,8]. It is reported that plasma cells originate from bursa of Fabricius[5,9,10,11]. These cells protect the eye against infections by producing antibodies as a primer response to local antigenic stimulation in the eye[11]. Thus, in the domestic avian birds, it is suggested that the Harderian gland is an alternative central lymphoid organ to the bursa of Fabricius[10]. The plasma cells of the avian in the Harderian gland have been localized at the interlobuler connective tissue. It is suggested that the B-lymphocytes made here migrate to the secondary lymphoid organs[4]. Rothwell et al., (1972)[12] found that poultry plasma cells resemble mammalian plasma cells ultrastructurally and have common histochemical properties[12].

It is suggested that bursectomy prevents the normal development of plasma cells in Harderian gland; and that it causes serum immunoglobulin levels and secretory immunoglobulins in the tears to decrease. Thus, it is thought that the Harderian gland has anactive role in fluid defense[13].

Harderian gland is a field for activation and terminal differentiation of B cells as well as the passage of different immunoglobulins and plasma cell proliferation seen in chickens[7,14,15,16,17,18,19]. Considering such different properties, the Harderian gland of chickens is thought to be a peripheral lymphoid organ participating

in local immunological responses[2]. Although there is evidence that the Harderian gland plays an important role in the protection of the chicken immune system, the information about the gland in other species of birds are inadequate or absent.

The purpose of this study is to investigate the relation of increase of the number of plasma cells in the Harderian gland of chukar Partridge (*Alectoris chukar*) with the development and involution periods of bursa of Fabricius through histological methods.

II. Material And Methods

Animals

In this study, Harderian glands and bursa of Fabricius of 20 3 month old (10 male, 10female), 20 6 month old (10 male, 10 female) brown partridges purchased from a commercialfarm (Turkey / Antalya) were used. Before starting the investigation, the study was approvedby Selcuk University Veterinary Faculty Ethical Committee (SÜVFEK) with decision dated25.03.2014 and numbered 2014/11. The animals were kept in natural light, humidity andtemperature conditions and allowed to consume water and food freely.

Histological Method

Harderian gland and bursa of Fabricius tissue samples, which were taken as total, weredetermined by keeping them in 10% neutral formaldehyde for 24 hours. Tissue fragmentswere blocked in paraffin following the known histological techniques such as washing,dehydration and polishing processes. 5 μm thick sections taken from the blocks weresubjected to the following procedures.

1-Triple staining technique of Mallory[20] modified by Crossman forgeneral histological examination.

2-Methyl Green-pyronin (MGP) staining method for the demonstration of plasma cells[21].The obtained preparations were examined by light microscobe (Leica DM2500,Switzerland); and the shapes of the required sites were taken with the camera attachment thesame microscope Leica DFC 320 (Switzerland).

Plasma cell counting

Plasma cell counting was separately performed for each sample for Harderian glandand bursa of Fabricius tissue samples of 3 and 6 month old chukar Partridges used in ourstudy. The counting and comparison of Harderian gland and bursa of Fabricius tissue samplesof an example was done with care. An objective micrometer (line micrometer) was used tocalculate the field of view of the microscope. In each sample, 10 randomly selected areas(each area 25434 μm) were counted and their averages were taken. Then, each group (3-month male-female and 6-month male-female) was separately averaged (Table I).

Statistical Analysis

The Mann-Whitney U test was used to determine the association of the numbers ofplasma cell with the groups. In this analysis, 3-month-old Harderian gland and bursa ofFabricius and 6-month-old Harderian gland and bursa of Fabricius, 3-month-old male andfemale Harderian gland and 3-month male and female bursa of Fabricius were separatelytested (Table II, III, IV).

III. Result

Histomorphology

Harderian gland in the chukar Partridges, It was seen that the palpebra tertia took place in the medial eye and was in association with this organ. It was determined that the Harderian glands of chukar Partridges were in dirty yellow colour, complied with the bulbus oculi, had a shape resembling uneven hemisphere and its surface was smooth. It was observed that the Harderian gland was not related to the cartilago palpebra tertiary (Figure 1a).

As with other avian species, in the chukar Partridges also, it was observed that bursa of Fabricius was embeded in the dorsal of the cloaca and it opened to cloaca via a channel. In addition, it was observed that bursa of Fabricius was surrounded by a capsule of connective tissue and was formed from tunica serosa, tunica muskularis, and tunica mucosa layers from the outside-in. It was observed that the tunica muscularis was composed of external longitudinal muscles and inner circular muscular smooth muscles. The tunica mucosa also plated into the lumen of the organ and was observed to be composed of 10-15 platelets. It was found that lamina epithelialis and lymph follicles were present in each plica. It was determined that lamina epithelialis was composed of two parts called as FAE and İFE. It was noted that the lymph follicles contained cortex and medulla sections and were separated with capillary vessel in some places with CMBC (Corticomedullary Border Cells) (Figure 1b).

Plasma cells

In Methil Green-pyronin staining method, the plasma cells were found around thecorpus glands and in connective tissue septums taking place immediately below the connective tissue capsule surrounding the Harderian gland of chukar Partridge (Figure 2a). A large number of plasma cells were also observed around the primary channels of the Harderian gland and around the main drainage channel (Figure 2b). The plasma cells in the Harderian gland of the six-month-old chukar Partridges were observed to be more than the plasma cells in the Harderian gland of the three-month-old chukar Partridge.

Plasma cells in the chukar Partridge bursa of Fabricius were encountered in connective tissue covering the organ, around the blood vessels and inside the follicles. It was observed that the number of plasma cells in the 3 month old chukar Partridge bursa of Fabricius was higher than that of 6 months bursa of Fabricius (Figure 3a, 3b).

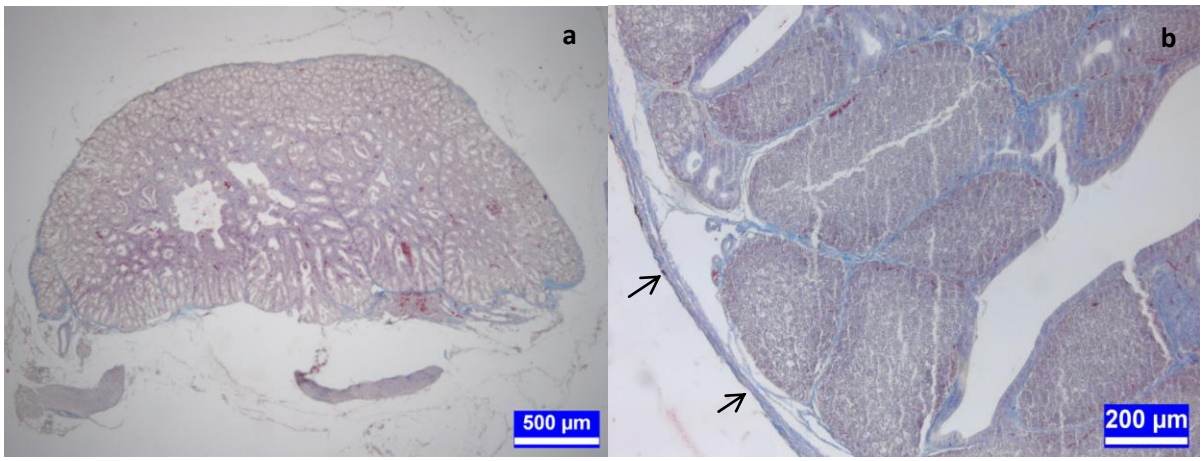

Figure 1: Half-shaped image of Harderian gland (a). The connective tissue capsule (arrows) that surrounds the organ externally in bursa of Fabricius, (b). Triple.

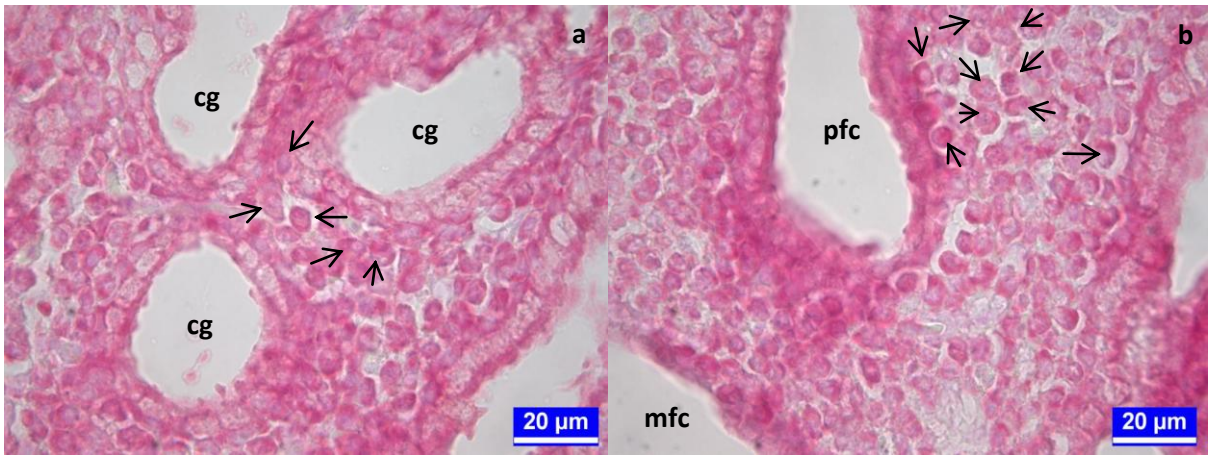

Figure 2: Three month old of chukar Partridge plasma cells (arrows) around the corpus glands (cg) in the Harderian gland (a). Plasma cells (arrows) around the primary flow channel (pfc) and main flow channel (mfc) in the six month old chukar Partridge Harderian gland (b). Methyl Green Pyronin.

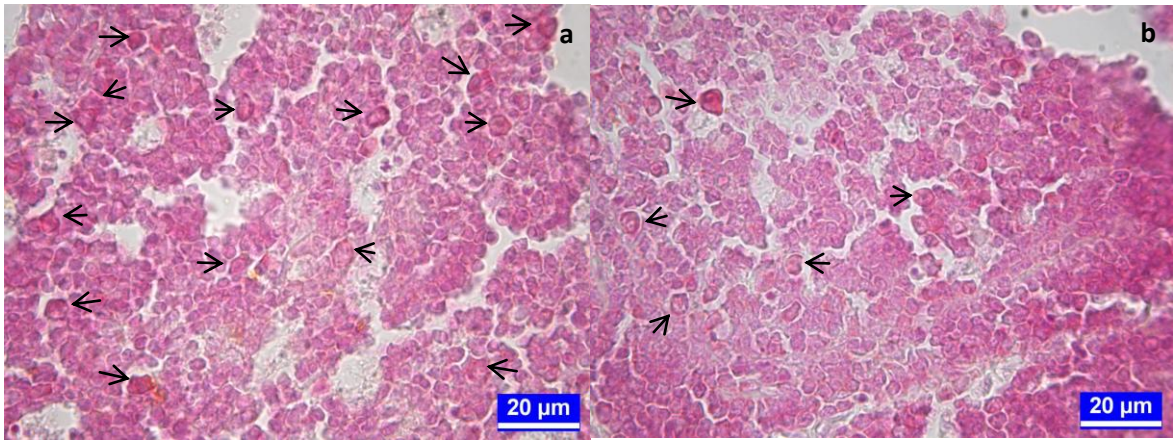

Figure 3: Plasma cells (arrows) (a) in the follicles in the three-month old chukar Partridge bursa of Fabricius. Plasma cells (arrows) located within the follicles in the six month chukar Partridge bursa of Fabricius (b). Methyl Green Pyronin.

Plasma cell count

The results obtained in the plasma cell counts performed in Harderian gland and bursa of Fabricius tissue samples of 3 and 6 month old chukar Partridges used in our study are given in Table 1.

Statistical Analysis

Statistical analysis of the plasma cell counts carried out for Harderian gland and bursa of Fabricius tissue samples of 3 and 6 month old chukar Partridges used in our study are given in the Table 2,3,4.

Table no1:. Average of the plasma cell numbers in the chukar Partridge Harderian gland and bursa of Fabricius.

	Harderian Gland		**Bursa Fabricius**	
Gender Age	**Male** ($\bar{X}$ ±S)	**Female** ($\bar{X}$ ±S)	**Male** ($\bar{X}$ ±S)	**Female** ($\bar{X}$ ±S)
3 Months	3,65±0,89	3,8±1,36	10,85±1,06	11,75±1,27
6 Months	6,99±0,88	6,45±1,15	3,78±0,43	3,8±0,44

Table no 2: Statistical analysis results between three and six month old Harderian gland and bursa of Fabricius.

Groups	**N**	**Median**	**p Value**
3 months Harderian gland	20	3,700	0,000
3 months bursa of Fabricius	20	11,050	
6 months Harderian gland	20	6,9000	0,000
6 months bursa of Fabricius	20	3,8000	

Table no 3: Statistical analysis results of plasma cell counts in three- and six-month-old female and male Harderian glands.

Genders	**n**	**Median**	**Ave Rank**	**Z**	**p Value**
3 months female Harderian gland	10	3,650	10,4	-0,08	0,940

3 months male Harderian gland	10	3,900	10,6	-0,08	
6 months female Harderian gland	10	6,850	9,6	-0,72	
6 months male Harderian gland	10	6,950	11,5	0,72	0,472

Table no 4: Statistical analysis results of plasma cell counts in three and six-month-old female and male Bursa of Fabricius.

Gender	n	Median	Ave Rank	Z	P Value
3 months female bursa of Fabricius	10	11,35	12,7	1,66	0,096
3 months male bursa of Fabricius	10	10,85	8,3	-1,66	
6 months female bursa of Fabricius	10	3,800	10,7	0,11	0,909
6 months male bursa of Fabricius	10	3,850	10,4	-0,11	

IV. Discussion

One of the most important features of the chicken Harderian gland is that it carries a large number of plasma cell populations depending on the age of the organism. Plasma cells are not observed so intensely in any organ of the avian. Therefore, this part is considered to be part of the "Head Associated Lymphoid Tissue" (HALT) system. The proliferative activities of plasma cells are thought to generate with the effect of the Harderian gland factor, which has a lymphokine-like effect[22].

In this study, it was observed that the number of plasma cells in the 6 month-old chukar Partridge Harderian gland was significantly higher than that of the 3 month-old chukar Partridge plasma cell.

In this study, plasma cells in the Hardian gland before and after involution of bursa of Fabricius were counted. Plasma cell count was observed to be higher in the 3 month-old chukar Partridge Harderian gland than 6 month-old chukar Partridge Harderian gland. The number of plasma cells in the three-month old chukar Partridge bursa of Fabricius was almost three times greater than that of the 6 month-old chukar Partridge bursa of Fabricius (Table I).

The number of plasma cells in the Harderian gland of three months old male and female chukar Partridge was very close to each other. There was no difference between the 3 month-old female and male bursa of Fabricius plasma cell counts. When 6 month-old female and male Harderian gland plasma cells were compared, values were observed to be close to each other. Again, 6 month-old female and male bursa of Fabricius plasma cell numbers were observed to be close to each other (Table I).

Unlike the bursa of Fabricius thymus, it is not only the primary lymphoid organ. The presence of a small T lymphocyte cluster (DIA) in the dorsal of the channel opening to the cloaca is also considered a sign of this. However, because the organ becomes atrophy in a short time and produces a low level of antibody, they are not important as secondary lymphoid organs.

In our study, we obtained findings that support the consideration of the Harderian gland as an alternative lymphoid organ to the bursa of Fabricius in the literature.

As can be seen in the Tables, the number of plasma cells in the bursa of Fabricius of 3 and 6 month-old chukar Partridges decreases, while the increase in the number of plasma cells in the Harderian gland compared to the same period gives hope for our researches that the Harderian gland is an alternative organ to bursa of Fabricius. For this purpose, we think that a research which will be carried out immediately after the incubation and during the periods when the bursa of Fabricius is completely invasive will shed much more light on whether the Harderian gland is an alternative organ to the bursa of Fabricius.

Findings in this study are also important for the quantitative determination of plasma cells in Harderian gland and bursa of Fabricius. As a result, findings from this study strengthen the view that the Harderian gland is an alternative organ to the bursa of Fabricius in the avian.

While Gulmez and Aslan (1999)[28] reported that the plasma cells are distributed homogeneously in the cortex and medulla of native goose bursa of Fabricius, Hodges (1974)[29]reported that plasma cells were not found in follicles in poultry, but in the follicles and the connective tissue under the epithelium. Sari and Kurtdede (2007)[30] reported that they found plasma cells in connective tissue in turkey bursa of Fabricius. In this study, plasma cells in 3 and 6 month old chukar Partridge bursa of Fabricius were found around the vein surrounding the organ, around the blood vessels and inside the follicles. It was observed that the plasma cells in the lymph follicles were homogeneously distributed in the cortex and medullary.

Butcher et al., (1989)[24] report that changes in involution observed in White Leghorn chickens bursa of Fabricius are different and are generally at the beginning of egg production, not related to age. In a study conducted on chickens[25], it was reported that the initial changes in involution in bursa of Fabricius reduced the weight of bursa of Fabricius and this was more pronounced in males. Mercer-Oltjen and Woodard (1987)[26]reported that there was no difference between male and female animals in terms of changes in weight loss or other involution of bursa of Fabricius in their study on chukar Partridges and pheasants. Ciriaco et al., (2003)[27] reported that atrophic or cystic follicles of significant involute changes begin to appear in the twentieth week, changes involving involution in chickens begin in approximately the eighth week, more pronounced changes occur in the twentyforth week, and that involution is completed within approximately 26 weeks. In this study, it was also observed that the first changes related to involution in 3 month-old chukar Partridges started with the depressions in the epithelium cells of the İFE and FAE. In six-month old chukar Partridges, however, marked cystic follicles surrounded by epithelium were found. It was also observed that the plicks disappeared, the number and volume of the lymph follicles decreased, the lumen narrowed considerably, and the connective tissue mass increased.

Following involution, the researchers[23], who reported histological changes indicative of involution in bursa of Fabricius onset at 10th and 12th weeks andinvolution resulting in organ atrophy occurred in early involution phase (90-150 days), late involution phase (up to 165 days) and residual phase (165- 180 days), noted that there is a clear difference between the degree of involuntary changes observed both in the individual and in the lymph follicles of the same bursa of Fabricius when the time of onset of the first histological manifestation of this regression event in the organism is taken into account. In this study, in some three months (90-120 days) bursa of Fabricius chukar Partridge, changes in involution in FAE and occasionally FAE were observed.

Wight et al., (1971)[5] and King and McLelland (1984)[11] report the presence of plasma cells derived from bursa of Fabricius in the Harderian gland. These cells produce antibodies in response to priming in the presence of local antigenic stimulation, thus they protect the eye from infections[11]. In addition to this, it is suggested that in the domestic avian, the Harderian gland is an alternative central lymphoid organ to the bursa of Fabricius[10]. Plasma cells in the Harderian gland of the avian are localized in the interlobular ligament. It is suggested that the B-lymphocytes made here migrate to the secondary lymphoid organs[4,6,15]. The number of plasma cells in interstitial connective tissue significantly increases in older animals. It has been reported that in the domestic poultry, in the lamina propria of the organ, there are plasma cell infiltrations with increasing numbers of age, and Russell bodies in different stages of the development of the majority of these cells are detected[22]. Researchers[12] found that plasma cells in poultry have ultrastructural similarities to mammals and have common histochemical characteristics. It is also mentioned that the plasma cells in the hard-ware are able to synthesize IgA[32,33,34], Ig G [33,34] and that the gland is the most important organ in the production of lacrimal IgA against Newcastle virus.

According to the findings, 3 and 6 month-old of Harderian gland and bursa of Fabricius were not found statistically significant in plasma cell counts (among male and female ones) (Table III, IV, $p > 0,05$). The relationship between three and six months (male + female) Harderian gland; 3 and 6 month-old (male + female) bursa of Fabricius plasma cell counts was found to be statistically significant at high level (Table II, $p < 0.001$).

V. Conclusion

In our study, we obtained findings that support the consideration of the Harderian gland as an alternative lymphoid organ to the bursa of Fabricius in the literature. As can be seen in the Tables, the number of plasma cells in the bursa of Fabricius of 3 and 6 month-old partridges decreases, while the increase in the number of plasma cells in the Harderian gland compared to the same period gives hope for our researches that the Harderian gland is an alternative organ to bursa of Fabricius. For this purpose, we think that a research which will be carried out immediately after the incubation and during the periods when the bursa Fabricius is completely invasive will shed much more light on whether the Harderian gland is an alternative organ to the bursa Fabricius.

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References

[1]. Payne, A.P., 1994. The Harderian gland: a tercentennial review. J. Anat. 185, 1–49.
[2]. Shirama, K., Satoh, T., Yokoyama, Y., Kano, K., Kitamura, T., Yamada, J., 1996. Ultrastructural study on the Harderian gland of the rabbit (Oryctolagus cuniculus). Fol. Morp. 55, 133-141.
[3]. Ashok, P., Venkatkrishnan, A., Vijayaragavan, C., Ramkrishna, V., 2000. Gross morphology and biometrical study of the Harderian gland in White Leghorn birds. Indian J. Anim. Sci. 15, 217–219.
[4]. Bang, B.G., and Bang, F.B., 1968. Localized Lymphoid Tissues and Plazma Cells in Paraocular and Paranasal Organ Systems in Chickens. Am. J. Pathol. 53, 735-751.
[5]. Wight, P.A.L., Burns, R.B., Rothwell, B., Mackenzie, G.M., 1971. The Harderian gland of the domestic fowl. I- Histology with reference to the genesis of plazma cells and Russell bodies. J. Anat. 100, 307-315.
[6]. Aitken, I.D. and Survashe, B.D., 1977. Plazma cells in Vertebrate Paraocular Glands. Int. Archs. Allrg. Appll. Immunol. 53, 62-67.
[7]. Mansikka, A., Sandberg, M., Veromaa, T., Vainio, O., Granfors, K., Toivanen, P., 1989. B cell maturation in the chicken Harderian gland. J. Immunol. 142, 1826–1833.
[8]. Altunay, H. and Kozlu, T., 2004. The fine structure of the Harderian gland in the ostrich (Struthio camelus). Anat. Histol. Emb. 33, 141-145.
[9]. Burns, R.B. 1975. Plazma cells in avian Harderian glands and morphology of the gland in the rock. Can. J. Zool. 53, 1258- 1269.
[10]. Glick, B., and Olah, I., 1981. Gut-associated-lymphoid tissue of the chicken. Scan. Elect. Micros. 3, 99-108.
[11]. King, A.S., and Mclelland J., 1984. Birds their structure and function. Baillière Tindall, Londra, Philadelphia.
[12]. Rothwell, B., Wight, P.A.L., Burns, R.B., Mackenzie, G.M., 1972. The Harderian glands of the domestic fowl. III. Ultrastructure. J. Anat. 112, 233-250.
[13]. Chieffi, G., Baccari, G.C., Dimatteo, L., Distria, M., Minucci, S., Varriale, B., 1996. Cell biology of the Harderian gland. Int. Rev. of Cytol. 168, 1- 79.
[14]. Gallego, M., and Glick, B., 1988. The proliferative capacity of the cells of the avian Harderian gland. So Dev Comp. Immunol. 12, 157-166.
[15]. Savage, M.L., Olah, I., Scott, T.R., 1992. Plasma cell proliferation in the chicken Harderian gland. Cell Prolif. 25, 337–344.
[16]. Scott, T.R., Savage, M.L., Olah, I., 1993. Plazma Cells of the Chickens Harderian Gland. Poul Sci. 72, 1273-1279.
[17]. Tsuji, S., Baba, T., Kawata, T., Kajikawa, T., 1993. Role of Harderian gland on differentiation and proliferation of immunoglobulin A-bearing lymphocytes in chickens. Vet. Immunol. Immunopathol. 37, 271–283.
[18]. Olah, I., Kupper, A., Kittner, Z., 1996. The lymphoid substance of the chickens Harderian gland is organized in two histologically distinct compartments. Microsc. Resarch Tech. 34, 166–176.
[19]. Koskela, K., Kohonen, P., Nieminen, P., Buerstedde, J.M., Lassila, O., 2003. Insight into lymphoid development by gene expression profiling of avian B cells. Immunogenetics 55, 412–422.
[20]. Mallory FB, 1900. A contribution to staining methods: I. A differential stain for connective-tissuefibrillae and reticulum. J Exp Med, 5, 15-20.
[21]. Pappenheim A, 1899. Vergleichende Untersuchungen über die elementare Zusammensetzung desRothen Knockenmarkes einiger Säugenthiere. Virchows Archiv fur Pathologische AnatomiePhysiologie, 157, 19.
[22]. Scott TR, 1996. Immune cell proliferation in the Harderian gland: an avian model. Microsc Res Tech,34, 149- 155.
[23]. Kocaöz, N., Çelik İ., Ünsal, S., 1997. Tavuk bursa Fabricii'sinin embriyonel gelişmesi üzerine ışık mikroskobik çalışmalar. SÜ Vet. Sci. J. 13, 43-51.
[24]. Butcher, G.D., Harms, R.H., Winterfield, R.W., 1989. Relationship between delayed onset of egg production and involution of the bursa of Fabricius in White Leghorn chickens. Avi. Dis. 33, 361–4.
[25]. Milicevic, Z., Vujic, D., Isakovic, K., Micic, M., Milicevic, N.M., 1986. Involution of bursa of Fabricius in male and female chickens: a light microscopic histoquantitative study. Poult. Sci. 65, 18-23.
[26]. Mercer-Oltjen, S.L., and Woodard, A.E., 1987. Development of the bursa of Fabricius in the partridge and pheasant. Poult. Sci. 5, 413–21.
[27]. Ciriaco, E., Pinera, P.P., Diaz-Esnal, B., Laura, L., 2003. Age-related changes in the avian primary lymphoid organs (thymus and bursa of Fabricius). Microsc. Res. Techniq. 62, 251-253.
[28]. Gülmez, N., and Aslan, S., 1999. Histological and Histometrical Investigations on Bursa of Fabricius and Thymus of Native Geese. Tr. J. of Vet. and Anim. Sci. 23, 163-171.
[29]. Hodges, R.D., 1974. The Histology of the Fowl. 2nd ed. Academic Press, London, UK. 205-21 pp.
[30]. Sarı, E.K., and Kurtdede, N., 2007. Light and Electron Microscopic Studies of the Bursa of Fabricius in Turkeys. Kafkas Unv. Vet. Fac. J. 13, 177-184.
[31]. Scott, T.R., 1996. Immune cell proliferation in the Harderian gland: an avian model. Microsc. Res. Techniq. 34, 149- 155.
[32]. Mueller, A.P., Sato, K., and Glick, B., 1971. The chicken lakrimal gland, gland of Harder, caecal tonsil, and accessory spleens as sourches of antibody producing cells. Cell Immunol. 2, 140-152.
[33]. Russel, P.H., 1993. Newcastle disease virus: Virus replication in the Harderian gland stimulates lakrimal Ig A; the yolk sac provides early lakrimal Ig G. Vet. Immunol. Immunopathol. 37, 151-163.
[34]. Russel, P.H., and Koch, G., 1993. Local antibody forming cell responses to the Hitcher B1 and Ulster strains of Newcastle disease virus. Vet. Immunol. Immunopathol. 37, 165-180.

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