Assiut Vet. Med. J. Vol. 36 No. 72, January 1997

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DEVELOPMENT OF THE FETAL RABBIT LUNG

(With 1 Table & 18 Figures)

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(Received at 25/12 /1996)

تطور رئة جنين الأرنب

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أجرى هذا البحث للتعرف على التغيرات المورفولوجية التى تحدث فى رئة ٣٥ من أجنة الأرانب البلدى التى تتراوح أطوالها من ١٥ – ١٣٠مم . ولقد تبين من الدراسة أنه فى المرحلة الجنينية الأولى تكون الرئة صغيرة الحجم وتقع فى الجزء الخلفى الظهرى من التجويف الصدرى، ثم تزداد فى الحجم بتقدم العمر لتشغل معظم التجويف الصدرى . فى الأجنة التى يبلغ طولها من ١٥ – ٢٥مم تتكون الرئة من أنيبيبات أولية موجودة فى كتلة من النسيج الضام الجنينى . وفى الأجنة التى تتراوح أطوالها من ٤٠ – ٧٠مم أمكن تمييز فصوص الرئة وكذلك الشريان والوريد الرئوى ، وتمت الأنيبيبات السابقة وانقسمت الى أنيبيبات صغيرة أمكن تمييزها الى نوعين أحدهما يعطى الممرات الهوائية المستقبلية والأخر يعطى الجزء التنفسى (السنخى) المنتظر . وعند طول ٨٠ – ١٠٥مم أصبحت فصوص الرئة واضحة وازدادت الأنيبيبات السنخية فى العدد والحجم واتصلت مع بعضها مكونة قنوات سنخية مبطنة بخلايا طلائية ذات أشكال مختلفة ، كما تميزت هذه المرحلة بنقص كمية النسيج البينى . وفى المرحلة الأخيرة من الحمل (١١٠ – ١٣٠مم) تميزت الخلايا المبطنة للحويصلات الأولية الى خلايا ظلائية حويصلية من النوع (١) والنوع (٢) ، كما لوحظ العديد من الأوعية الدموية منغمسة فى النسيج الظلائى المبطن لهذه الحويصلات . ولقد أوضحت الدراسة أن ارتفاع الخلايا الظلائية المبطنة للجزء التوصيلى والتنفسى لرئة جنين الأرنب يتناقص بتقدم العمر .

SUMMARY

The morphogenesis of the fetal rabbit lung (15-130 mm CVRL) was studied. In rabbit fetuses of 15-25 mm CVRL, the lung is relatively small lying in the caudodorsal part of the thoracic cavity. It is represented by primitive tubules embedded in mesenchymal connective tissue mass. On reaching 40-70 mm CVRL, the lobation of the lung is recognized. The visceral pleura is reflected on the pulmonary root to continue with the parietal pleura. The pulmonary artery and vein are differentiated. The primitive tubules grow and divide

resulting in smaller orders. Two types of tubules can be demonstrated; the future bronchial and acinar tubules. In rabbit fetuses of 80-105 mm CVRL, the lobes are well distinct and separated by deep interlobar fissures. The acinar tubules communicate forming acinar canals which are lined by epithelial cells of different shapes. The interstitial connective tissue reduces in amount and becomes more condensed. In rabbit fetuses of 110-130 mm CVRL, the lung occupies most of the thoracic cavity. The primitive alveoli are lined by two types of cells; alveolar epithelial cell type I and II. Many blood capillaries insinuate within the lining epithelium of alveoli. Disintegrated and sloughed epithelial cells are demonstrated in the conducting portion of the lung. The morphometric study indicates that the height of epithelium of both conducting and respiratory portions of fetal rabbit lung is decreased with the advancement of age.

Key words: Development, rabbit lung

INTRODUCTION

The prenatal development of the lung had been the subject for several investigators in different species (Latimer, 1949; Loosli and Potter, 1959; Balis and Conen, 1964; Kikkawa et al., 1968; Ten Have-Opbroek, 1979; Alcorn et al., 1981; Farrel, 1982; Awad, 1985; Osman et al., 1986; Nosseur et al., 1987 and Sayed, 1994). However, the fetal lung of the rabbit received a little attention of investigators, in spite of this animal is considered to be one of the most important experimental animals. Therefore, this work was undertaken to give more macroscopical and microscopical informations on the development of the fetal lung of the balady rabbits.

MATERIAL and METHODS

The present work was carried out on 35 apparently normal rabbit fetuses of both sexes ranging from 15-130 mm CVRL. The fetuses were divided into four groups; the first group was ranged from 15-25 mm CVRL, the second from 40-70 mm CVRL, the third from 80-105 mm CVRL and the fourth group from 110-130 mm CVRL. Each group from the first three included nine specimens and the last group included eight pecimens. The fetuses were collected from the pregnant rabbits (balady species), which were anesthetized with chloroform and injected with fixative (10% neutral buffered formaline and Bouin's fluid) through the common carotid artery,

then their uteri were removed and the fetuses were dissected free. The entire fetuses of 10-40 mm CVRL and the lung tissue of the other fetuses were taken and immersed in the fixative solution. Paraffin sections of 5-7 µm were prepared as usual and stained with Haematoxylin and Eosin, Periodic acid schiff, Alcian blue and Weigert's elastic stain (Drury and Wallington, 1980).

Small pieces of the fetal lung tissue were fixed in paraformaldehyde-glutaraldehyde fixative (Karnovsky, 1965). After osmication the tissue were washed in cacodylate buffer, dehydrated in ethanol followed by propylene oxide then embedded in araldite. Semithin sections were cut at 1 µm thickness and stained with Toluidine blue.

Using Quantiment Q 500 MC image processing and analysis system (Leica) the height of the lung epithelium of eight fetuses from each group were measured, and the mean values were recorded.

RESULTS

In rabbit fetuses of 15-25 mm CVRL, the developing lung is relatively small in size lying in the caudodorsal part of the thoracic cavity, while the rest of this cavity is occupied by the large-sized developing heart. The lung is related dorsally to the roof of the thoracic cavity, cranioventrally to the heart and is separated caudally from the stomach and liver by the Septum transversum (Fig.1).

The developing right and left lungs evaginate laterally into the corresponding prospective pleural cavity, thus they are surrounded from the outside by the splanchnic mesoderm which represents the primitive visceral pleura. While the somatic mesoderm which lines the pleural cavity represents the primitive parietal pleura (Fig.1). At this stage, four buds were observed in the right lung and two in the left lung. These buds represent the future pulmonary lobes.

The light microscopical observations reveals that in this period of intrauterine life (primitive stage), the lung is represented by primitive tubules embedded in mesenchymal connective tissue (Fig. 1). The tubules are lined by undifferenitated pseudostratified columnar epithelium which measures 19.81 µm in height. (Fig. 2,3). The epithelial cells have vacuolated cytoplasm. Strong PAS positive reaction is demonstrated within the cells lining the primitive tubules (Fig.4).

The mesenchymal connective tissue presents thin-walled blood spaces. They are lined by a single layer of flattened cells representing the primitive endothelium. These spaces contain blood cellular elements, most of them are

nucleated (Fig. 2). Mitotic divisions are occasionally demonstrated. The lung is surrounded from the outside by a single layer of low cuboidal or flattened mesothelial cells representing the primitive visceral pleura.

At this developmental stage, it was observed that the mesenchymal connective tissue is densely arranged in the periphery than on the center. Moreover, the blood spaces are demonstrated more at the periphery than at the center.

In the rabbit fetuses of 40-70 mm CVRL, The lung increases in size on the expense of the heart. It occupies the dorsal part of the thoracic cavity extending from the future diaphragm caudally to terminate slightly behind the thoracic inlet cranially (Fig. 6).

Craniomedially to the lung, the visceral pleura is reflected on the pulmonary root to continue with the parietal pleura. The latter pleura forms with that of the opposite side the primitive mediastinum, it is reflected caudally on the future diaphragm forming the diaphragmic pleura and on the future pericardium forming the pericardial pleura (Fig.6,7).

The right lung is sligtly larger than the left one. The lobation of the lung is recognized and the lobes are separated from each other by interlobar fissures (Fig.5). The right lung divides into four lobes; cranial, middle, caudal and accessory. The caudal lobe is the largest, the cranial and middle lobes are nearly equal in size, while the accessory lobe is the smallest one. The left lung divides into two lobes; cranial and caudal. The former lobe is smaller than the latter one.

During this developmental stage (pseudoglandular stage), the lung has a glandular appearance (Fig.6). The lobar bronchi are surrounded by cartilagenous platelets (Fig.7). The tubules which are considered the primordial tubular system of the lung grow and divide giving rise to several order of smaller tubules. Two types of tubules can be demonstrated at this developmental period (Fig.8). The first type is characterized by wide lumen, single layer of columnar epithelium with basaly located large vesciular nuclei and paler cytoplasm. These tubules are relatively numerous than the other tubules. This type of tubules gives the prospective respiratory portion (future acinar tubules) of the lung.

The second type of tubules (Fig.8,9) is characterized by narrow irregular star-shaped lumen, the epithelium shows pseudostratified appearance and rest on distinct basement membrane. The epithelium of this type is higher than that of the other type (Table 1). The tubules are surrounded by thin layer of fusiform or spindle-shaped cells with oval or elongated nuclei (myoblastic cells) which are the primordia of the smooth

muscle cells. This type of tubules gives the prospective conducting portion (future bronchial tubules) of the lung.

At this stage, the lung shows high mitotic divisions (Fig.9). The lining epithelium of the future bronchial tubules presents some disintegrated and slouphed cells.The pulmonary root contains differentiated pulmonary artery and vein (Fig.7). The pulmonary artery lies dorsal to the vein and contains non-nucleated blood cellular elements. The thin-walled blood vessels are increased in number and size than the previous stage, most of them contain non-nucleated blood cellular elements.

In the rabbit fetuses of 80-105 mm CVRL, the lung extends from the thoracic inlet cranially to the diaphragm caudally. It extends also ventrally to envelop the heart dorsally and caudally.

The lobes of the lung are well distinct and are separated from each other by deep interlobar fissures. In case of the right lung, the cranial and middle lobes are separated from the caudal lobe by transverse fissure which extends from the dorsal border to the ventral border of the lung. The cranial lobe is separated from the middle one by longitudinally directed fissure which extends from the preceding fissure cranially till the cardiac notch (Fig.5). The accessory lobe extends medially to lie in the median plane caudal to the heart and ventral to the esophagus. The cranial and caudal lobes of the left lung are separated by caudoventrally directed fissure.

At this intrauterine period, the cardiac impression is distinct in the cranial and middle lobes of the right lung and in the cranial lobe of the left lung. The cardiac notch is larger on the left side than on the right one.

At this developmental stage (canalicular stage), the microscopical investigation shows that the acinar tubules are increased in number in relation to the bronchial ones. The acinar tubules communicate with each other forming elongated canals called acinar canals separated by interstitial tissue (Fig.10). These canals present irregular outlines. The lining epithelial cells of the acinar canals show different shapes. They are rounded, cuboidal and or pyramidal in shape with lightly stained cytoplasm. Their nuclei are large, rounded or oval in shape (Fig.10). The vasculature of the fetal rabbit lung is increased, and some of the blood capillaries appear in close contact with the lining epithelium. The interstitial connective tissue reduces in amount and becomes more condensed.

In this stage, the lining epithelium of the bronchiole presents more disintegrated and sloughed epithelial cells (Fig.11). It is surrounded by well differenitated smooth muscle fibers. The bronchial mucosal folds are higher than those of the previous stage (Fig.12).

In the rabbit fetuses of 110-130 mm CVRL, the lung is markedly increased in size in relation to the heart compared with the previous stages. Therefore, the lung occupies most of the thoracic cavity. It acquires its conical shape with the apex directed forwards. The base is concave to adapt the convex cranial surface of the diaphragm. The outer surface is convex as it lies against the thoracic wall, on the contrary the inner surface is concave.

The right lung is larger than the left one (Fig.13). The cranial lobe of the right lung is nearly quadrilateral in outline. The middle lobe of the right lung, the cranial lobe of the left lung and the caudal lobes of both lungs are triangular in shape (Fig.5,13). The accessory lobe is bean shape. The caudal lobe of each the right and left lung is separated from the other lobes by deep interlobar fissure. The fissures of both sides are situated nearly at the same level slightly caudal to the tracheal bifurcation.

At this developmental stage (alveolar stage), the primitive lung alveoli show two types of cells, the alveolar epithelial cells type I and II. The alveolar epithelial type I is represented by small flattened cells. The alveolar epithelial type II is large polyhedral cells contain large rounded vesicular nuclei, and their cytoplasm shows vacuoles of different sizes (Fig.14,15).

The bronchiole are lined by low columnar epithelium, partially ciliated (Fig.15). This epithelium shows large number of disintegrated and sloughed cells. Some cells are protruded from the surface into the lumen, these cells have narrow basal part and wide apical part. The cytoplasm of the aforementioned cells shows vacuoles, their nuclei are located apically (Fig.15, 16).

During this period, the reduction and condensation of the interstitial connective tissue is more than those in the preceding stage. This tissue shows numerous blood capillaries, most of them are insinuated within the lining epithelium of the alveoli (Fig.16). The cells are weakly stained with the PAS technique.

Table (1) and Fig. (17,18) indicate that, the height of the epithelium of both the conducting and respiratory portions of the rabbit lung is decreased towards the term of gestation period, where it reaches its lowest value. It was observed that the rate of decrement of the epithelium is more in the respiratory portion than in the conducting one.

Table (1): Mean values of the height of epithelium (μm) of conducting and respiratory portions of fetal rabbit lung at different stages.

Height of epithelium of:	15 - 25 mm (CVRL)	40 - 70 mm (CVRL)	80 - 105 mm (CVRL)	110 - 130 mm (CVRL)
Conducting portion	19.81±0.14*	16.06±0.16	12.44±0.13	10.97±0.09
Respiratory portion	19.81±0.14*	14.01±0.15	9.02±0.10	2.94±0.06 (I)** 7.72±0.11 (II)

* Height of epithelium of primitive tubules which are the same in both cases.
** (I) = alveolar epithelial cell type (I).
(II) = alveolar epithelial cell type (II).

DISCUSSION

The present work shows that, at the early embryonic stage (15-25 mm CVRL) the fetal rabbit lung occupies the caudodorsal part of the thoracic cavity. While, the rest of this cavity is occupied by the large-sized heart. With the advancement of age the lung increases in size on the expense of the heart. Therefore, the lung extends cranially to reach the thoracic inlet and ventrally to envelop the heart. Towards the end of gestation period the lung occupies most of the thoracic cavity. This indicates that, in the rabbit fetuses there is a reverse relation between the size of the lung and that of the heart. These findings are confirmed in camel fetuses by Sayed (1994), who stated that the volume and mass of the heart exceeds that of the lung at early embryonic stage. These parameters of growth are much faster in the lung than that of the heart towards term of gestation period. Latimer (1949) obtained nearly a similar result in dog fetuses. In addition, Hislop et al. (1984) mentioned that in the fetal monkeys, the lung volume increases linearly with body weight and gestation period.

The present study reveals that, in the rabbit fetuses of 15-25 mm CVRL, the developing lung evaginates laterally into the corresponding respective pleural cavity, thus it is surrounded from the outside by primitive visceral pleura (splanchnic mesoderm). While, the primitive parietal pleura (somatic mesoderm) lines the pleural cavity. A similar description was reported in domestic animals by Hare (1975) and in human by Sadler (1990). It was observed that in the rabbit fetuses of 40-70 mm CVRL, the visceral

pleura is reflected on the primitive pulmonary root to continue with the parietal pleura.

According to Thakur and Puranik (1984) as well as Mclaughlin and Chiasson (1990) the right lung of the adult rabbit is divided into four lobes; cranial, middle, caudal and accessory, however, the left lung is divided into two lobes, cranial and caudal. This lobation can be recognized in the examined rabbit fetuses of 40-70 mm CVRL. On the other hand, the latter authors added that the cranial lobe of the left lung is partially divided by incomplete fissure into two portions. This feature was not demonstrated in the fetal rabbit lung of the present work.

The present investigation indicates that the right lung of the fetal rabbit is larger than the left one. This difference in size is attributed to that the right lung includes an additional middle and accessory lobes.

On reaching 80-105 mm CVRL, the accessory lobe of the right lung becomes larger in size, thus it extends medially to lie in the median plane caudal to the heart. This results are in agreement with those recorded in the adult rabbit by Thakur and Puranik (1984).

In the rabbit fetuses of 15-25 mm CVRL (primitive stage), the fetal rabbit lung is represented by primitive tubules embedded in mesenchymal connective tissue mass. These tubules are lined by undifferentiated pseudostratified columnar epithelium as pointed out by Sayed (1994) in camel fetuses of 38-40 mm CVRL. On the other hand, these tubules are lined by stratified columnar epithelium as recorded in camel by Awad (1985) and in goat by Nosseur et al. (1987).

The present results show that, in the primitive stage the mesenchymal connective tissue is densely arranged in the periphery of the fetal rabbit lung than in the center. This explains that during this period the periphery of the lung shows delay in maturation than the center. This condition is noted by Kikkawa et al. (1968) in the canalicular stage of rabbit lung.

In the rabbit fetuses of 40-70 mm CVRL (pseudoglandular stage), the primitive tubules of the fetal rabbit fetuses grow and divide resulting in several order of smaller tubules. Two types of tubules can be demonstrated at this stage. They represent the prospective conducting portion (future bronchial tubules) and the respiratory portion(future acinar tubules). A similar result was reported in fetal rat by Ten Have-Opbroek (1991). On the contrary, the two types of tubules were described by Sayed (1994) in the camel fetuses of 50 mm CVRL (early embryonic stage). The foregoing results support the opinion of Ten Have-Opbroek (1979, 1981) and Ten Have-Operoek et al. (1988), who considered that the bronchial and

respiratory portions of the lung originate from the separate part of the primordial tubular system.

The present work reveals that, in rabbit fetuses of 40-70 mm CVRL, the future bronchial tubules are surrounded by thin layer of myoblastic cells which are considered the progenitor of the smooth muscle cells. These results agreed those of Collet and Des-Biens (1974) in the rat, that the myoblastic cells and the fibroblasts probably originate from the same mesenchymal cells and their differentiation depends on the zone where they are located. On reaching 80-105 mm CVRL (canalicular stage), the bronchioles are surrounded by well differentiated smooth muscle fibers. These fibers seem to be the cause of the folding of the bronchial epithelium. Therefore, the bronchial mucosal folds are higher at this stage than those observed in the previous one.

During the canalicular stage, the appearance of the fetal rabbit lung is dramatically altered with rapid expansion of the acinar tubules which communicate with each other forming acinar canals. The vasculature of fetal rabbit lung is increased at this stage, similar to that recorded in sheep by Alcorn et al. (1981) and in buffalo by Osman et al. (1986). Moreover, the present findings show that some of the blood capillaries appear in close contact with the lining epithelium of the acinar canal. This result is confirmed by Kikkawa et al. (1968), who stated that at this stage a thin potential air barrier is already established in some areas of the rabbit lung.

At the last stage of development, the present study indicates that the primitive alveoli of fetal rabbit lung show two types of the alveolar epithelial cells; type I and II. The precursors of these cells are original columnar epithelial cells that line prospective alveoli in the fetal lung tissue. These findings support the view that both types of the alveolar epithelial cells are endodermal in origin (Low and Sampoio, 1957; Campiche et al., 1963; and Kikkawa et al., 1968). In contrast, Policard et al. (1957) thought that both cells are mesenchymal in origin. However, Balis and Conen (1964) claimed that a transformation of the mature type II cell into the type I cell occurs in the lung of rats and human.

The alveolar epithelial cells type I are flattened cells responsible for permitting gas diffusion through their cytoplasm (blood air-barrier). The type II cells are the producers of the surfactant, a complex lipid and protein substance. This substance forms a phospholipid coat on the alveolar membranes which prevents the collapse of the alveoli during expiration by reducing the surface tension at the air blood capillary interface (King, 1982 and Sadler, 1990).

The present investigation indicates that the quantity of the PAS positive material (mostly glycogen) is large at the early developmental stage of fetal rabbit lung, then it decreases towards term of gestation period. This is due to that in the early stages of development the fetuses need more energy for the tissue differentiation, this PAS positive material can be considered as an energy reservoir (Moustafa, 1996). These results agreed those reported in human by Snyder et al. (1985), who stated that the undifferentiated fetal lung epithelial cells contain large glycogen pools that decline in area as gestation proceeds.

In the studied rabbit fetuses, a number of disintegrated and sloughed epithelial cells are demonstrated in the conducting portion of the lung. At the last stage of development, some epithelial cells protrude from the surface into the lumen of the bronchiole, these cells have wide apical part and narrow basal part. It is clear that these cells enter the process of sloughing. A similar observation was noted in fetal camel lung by Sayed (1994) and in human tracheal epithelium by Rhodin (1966). The latter author indicated that, the sloughing of the cell is proceeded by swelling of its apical part, then it is retracted, pushed out and phagocytosed by macrophages which invade the epithelium from time to time.

The morphometric study shows that, in the fetal rabbit lung the height of epithelium of both the conducting and respiratory portions is decreased with the advancement of age. It reaches its lowest value at the last stage of gestation. The rate of decrement of the height of epithelium is more in the respiratory portion than in the conducting one. It is clear that, there is a reverse correlation between the height of epithelium of the rabbit lung and the fetal age.

REFERENCES

Alcorn, D.G.; Adamson, T.M.; Maloney, J.E. and Robinson, P.M. (1981): A morphologic and morphometric analysis of fetal lung development in the sheep. Anat. Rec., 201: 655-667.

Awad, A.A. (1985): Histological and histochemical studies on the lung of the developing one-humped camel (Camelus dromedarius). Thesis Fac. Vet. Med., Zagazig Univ., Egypt.

Balis,J.U. and Conen, P.E. (1964): The role of the alveolar inclusion bodies in the developing lung. Lab. Invest. 13: 1215-1229.

Campiche, M.A.; Gautier, A.; Hernandez, E.I. and Reymond, A. (1963): An electron microscope study of the fetal development of human lung. Pediatrics, 32: 976-994.

Collet, A.J. and Des-Biens, G. (1974): Fine structure of myogenesis and elastogenesis in the developing rat lung. Anat. Rec., 179: 343-360.

Drury, R.B.B. and Wallington, E.A. (1980): Carlton's histological technique. 4th ed. Oxford University Press. New York, Toronto.

Farrel, P.M. (1982): Morphometric aspects of lung maturation. In: lung development. Biological and clinical persepectives. New York. Academic Press, PP. 13-25.

Hare, W.C.D. (1975): General respiratory system in: Sisson and Grossman's the anatomy of the domestic animals. Rev. by Getty. 5th ed. W.B. Saunders Company, Philadelphia, London, Toronto.

Hislop, A.; Howards, S. and Fairweather, D.V.I, (1984): Morphometric studies on the structural development of the lung in Macaca fascicularis during fetal and postnatal life. J. Anat., 138: 95-112.

Karnovsky, M.J. (1965): A formaldehyde-glutaraldehyde fixative of high osmolarity for use in electron microscopy. J. Celll Biology, 27: 137A.

Kikkawa, Y.; Motoyama, E.K. and Gluck, L. (1968): Study of the lungs of fetal and newborn rabbits: Morphologic, biochemical and surface physical development. Am. J. Pathol. 52: 177-210.

King, R.J. (1982): Pulmonary surfactant. J. Appl. Physiol. Respir. Environ., Exercise Physiol., 53: 1-8.

Latimer, H.B. (1949): The prenatal growth of the heart and the lungs in the dog. Anat. Rec., 104: 287-298.

Loosli, C.G. and Potter, E.L.(1959): Pre-and postnatal development of the respiratory portion of the human lung. Am. Rev. Respir. Dis., 80: 5-23.

Low, F.N. and Sampoio, M.M. (1957): The pulmonary alveolar epithelium as an entodermal derivative. Anat. Rec., 127: 51-63.

Mclaughlin, C.A. and Chiasson, R.B. (1990): Laboratory anatomy of the Rabbit. 3th ed. Wm. C. Brown Publishers.

Moustafa, M.N.K. (1996): Developmental studies on the lung in dog (Early intrauterine life). Assiuut Vet. Med. J. Vol. 35 No. 2: 1-13.

Nosseur, H.M.; Basha, E.S. and Awad, A. (1987): Pre-natal study of the goat lungs. Zagazig Vet. J. Vol. XV, No. I. 70-94.

Osman, A.H.K.; Amin, M. and Enany, S. (1986): Micromorphological approach to the development of the fetal lung of the Egyptian water buffalo. Alex. J. Vet. Sci., Vol. 2, No. 2: 1-13.

Policard, A.; Collet, A. and Pregermain, S. (1957): Electron microscope studies on alveolar cells from mammls. Proc. European Reg. Conf. Electron Microscopy, Stockholm, Acad. Press, New York, P. 244.

Rhodin, J.A.G. (1966): Ultrastructure and function of the human tracheal mucosa. Am. Rev. Respir. Dis, 93: 1-15.

Sadler, T.W. (1990): Langman's medical embryology, 6th ed. Williams and Wilkins.

Sayed, R.A.H. (1994): Histomorphological studies on the development of the lung of one-humped camel. Thesis, Fac. Vet. Med., Assiut Univ., Egypt.

Snyder, J.M.; Mendelson, C.R. and Johnston, C.R. (1985): Pulmonary development in transition from intrauterine to extrauterine Life. In: Lung Biology in Health and Disease, G.H. Nelson, Marcel Decker, New York, pp. 19-46,.

Ten Have-Opbroek, A.A.W. (1979): Immunological study of lung development in the mouse embryo. II. First appearance of the great alveolar cell, as shown by immunofluroescence microscopy. Dev. Biol., 69: 408-423.

Ten Have-Opbroek, A.A.W. (1981): The development of the lung in mammals. An analysis of concepts and findings. Am. J. Anat., 162: 201-219.

Ten Have-Opbroek, A.A.W. (1991): Lung development in the mouse embryo. Exp. Lung Res., 17: 111-130.

Ten Have-Opbroek, A.A.W.; Dubbeldam, J.A. and Otto-verberne, C.J.M. (1988): Ultrastructural features of type II alveolar epithelial cells in early embryonic mouse lung. Anat. Rec., 221: 846-853.

Thakur, R.S. and Puranik, O.G. (1984): Rabbit: A mammalian type. S. Chand and Company LTD. RAM. Nagar, New Delhi-11005.

LEGENDS

Fig. 1: Sagittal section in rabbit fetus of 15 mm CVRL showing: lung (L), liver (R), heart (H), prospective pleural cavity (PC), Septum transversum (ST), visceral pleura (VP) and parietal pleura (PP). Notice: the lung lies in the caudodorsal part of thoracic cavity. (H&E., X 40).

Fig. 2: Developing lung in rabbit fetus of 15 mm CVRL showing: primitive tubules (PT), mesenchymal connective tissue (M) and blood space (B) contain nucleated blood elements. (H&E., X 500).

Fig. 3: Developing lung in rabbit fetus of 15 mm CVRL showing: primitive tubule (PT) lined by undifferentiated pseudostratified columnar epithelium (PS). (H&E., X 500).

Fig. 4: developing lung in rabbit fetus of 15 mm CVRL showing: Strong PAS positive reaction within the epithelium of the primitive tubules (PT). (PAS., X 500).

Fig. 5: Fotograph of the right lung in rabbit fetus of 40 mm CVRL (A), 100 mm CVRL (B) and 130 mm CVRL (C) showing: cranial lobe (1), middle lobe (2), caudal lobe (3) and heart (H).

Fig. 6: Sagittal section in rabbit fetus of 50 mm CVRL showing: pulmonary root (arrow), lobar bronchus (LB), pulmonary artery (A), pulmonary vein (V), diaphragmatic pleura (DP), pericardial pleura (CP), heart (H) and liver (R). (H&E., X 18).

Fig. 7: Pulmonary root in rabbit fetus of 50 mm CVRL showing: visceral pleura (VP), parietal pleura (PP), line of reflection on pulmonary root (arrow), pulmonary artery (A), pulmonary vein (V), lobar bronchus (LB) surrounded by cartilagenous platelets (C). (H&E., X 125).

Fig. 8: Lung in rabbit fetus of 50 mm CVRL showing: two types of tubules, future bronchial tubule (BT) and future acinar tubule (AT). (H&E., X 500).

Fig. 9: Lung in rabbit fetus of 50 mm CVRL showing: future bronchial tubule (BT) surrounded by myoblastic cells (MS). Notice: mitotic division (arrow). (H&E., X 500).

Fig. 10: Semithin section in fetal lung of 90 mm CVRL showing: acinar canal (AC) lining epithelium (E) and blood capillary (arrow). (Toluidine blue. X 1000).

Fig. 11: Semithin section in fetal rabbit lung of 90 mm CVRL showing: bronchiole(B), ciliated cell (arrow) and Sloughed cell (S). (Toluidine blue, X 500).

Fig. 12: Lung in rabbit fetus of 80 mm CVRL showing: bronchial mucosal folds (arrow). (H&E., X 63).

Fig. 13: Fotograph of the ventral aspect of lungs in rabbit fetus of 120 mm CVRL showing: right lung (R), cranial lobe (1), middle lobe (2), caudal lobe (3), accessory lobe (4), left lung (L), cranial lobe (5), caudal lobe (6) and heart (H).

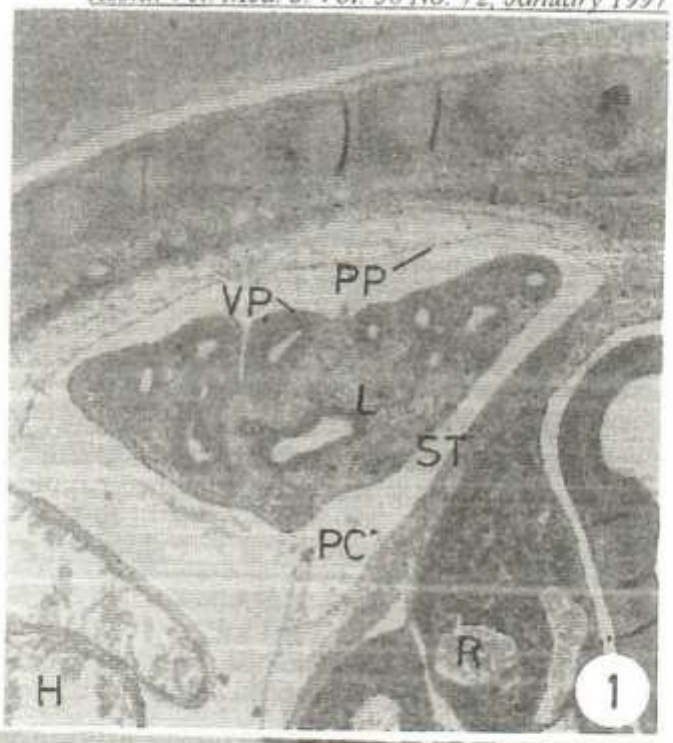
Fig. 14: Semithin section in fetal rabbit lung of 130 mm CVRL showing: primitive alveolus (AV) lined by alveolar epithelial cell type I(I) and type II(II). (Toluidine blue. X 1250).

Fig. 15: Semithin section in fetal rabbit lung of 130 mm CVRL showing: alveolar epithelial cells type I (I) and type II(II), bronchiole (B), ciliated cell (arrow), and disintegrated cell (D). Notice: ciliated cells in lining epithelium of bronchiole. (Toluidine blue, X 1250).

Fig. 16: Semithin section in fetal rabbit lung of 120 mm CVRL showing: bronchiole (B), disintegrated cell (D) with wide apical part and narrow basal part. Notice: blood capillaries insinuate within the alveolar epithelium (arrow). (Toluidine blue, X 630).

Fig. 17: Histogram showing the height of epithelium (μm) of the conducting portion of the fetal rabbit lung at different stages.

Fig. 18: Histogram showing the height of epithelium (μm) of the respiratory portion of the fetal rabbit lung at different stages. Notice: In 110-130 mm CVRL, the two columns represent alveolar epithelial cell type I and II.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R
H
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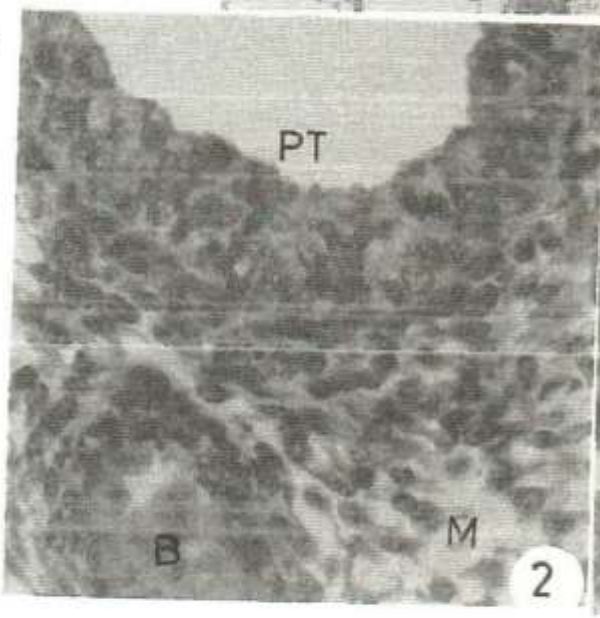
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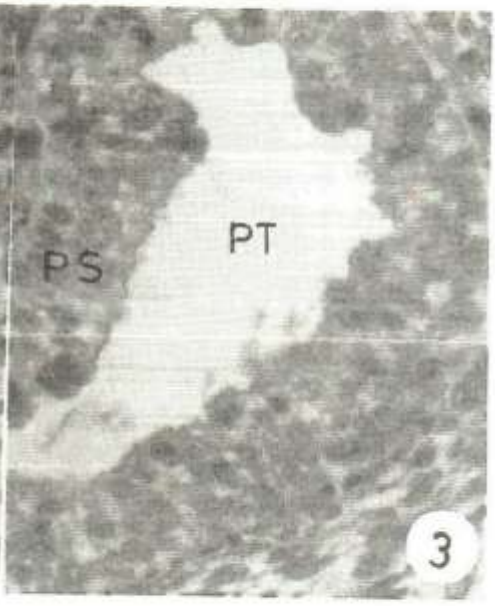
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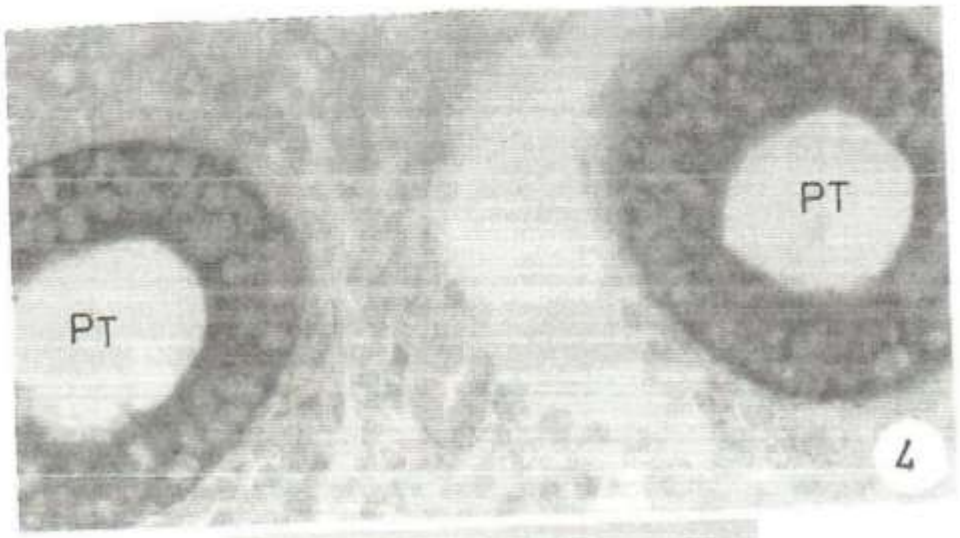
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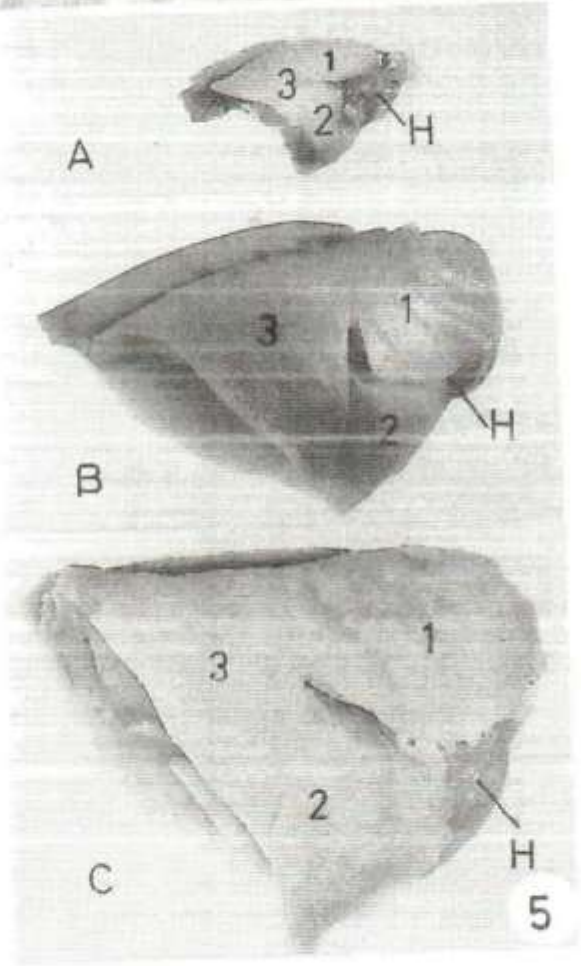
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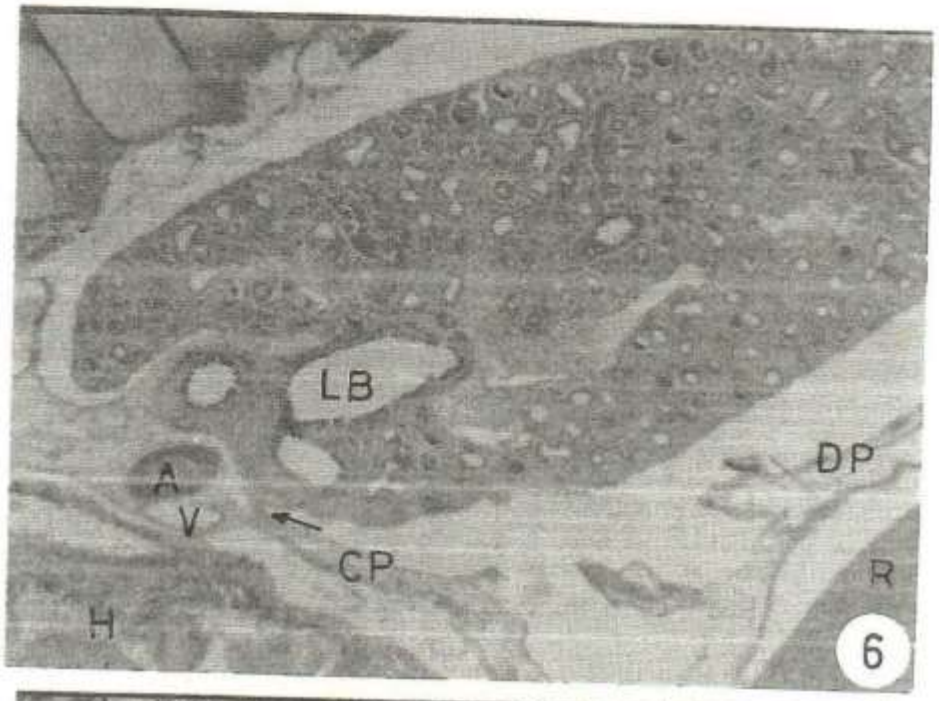
2
3
H
B
1
2
3
H
C
1
2
3
H
5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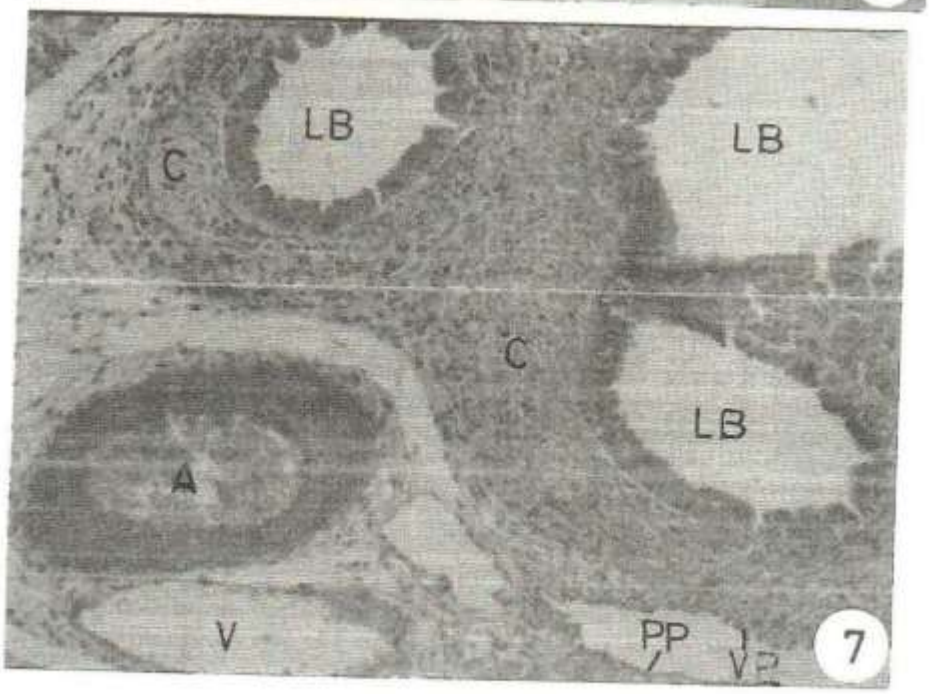
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A
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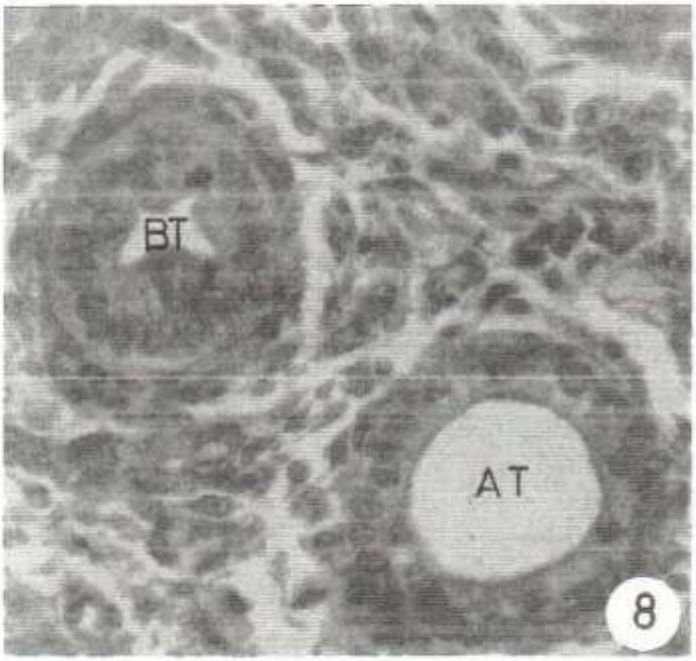
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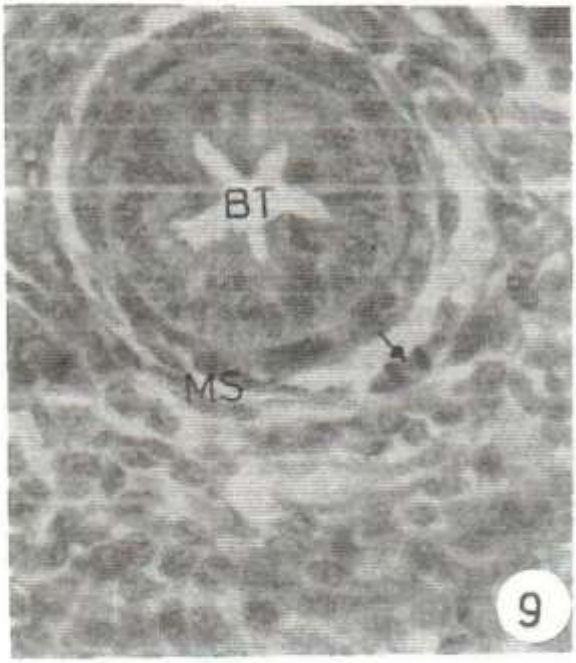
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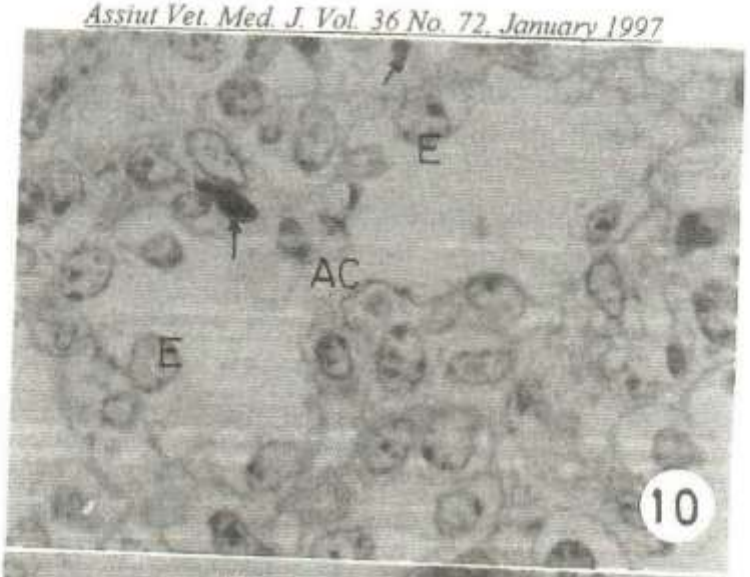
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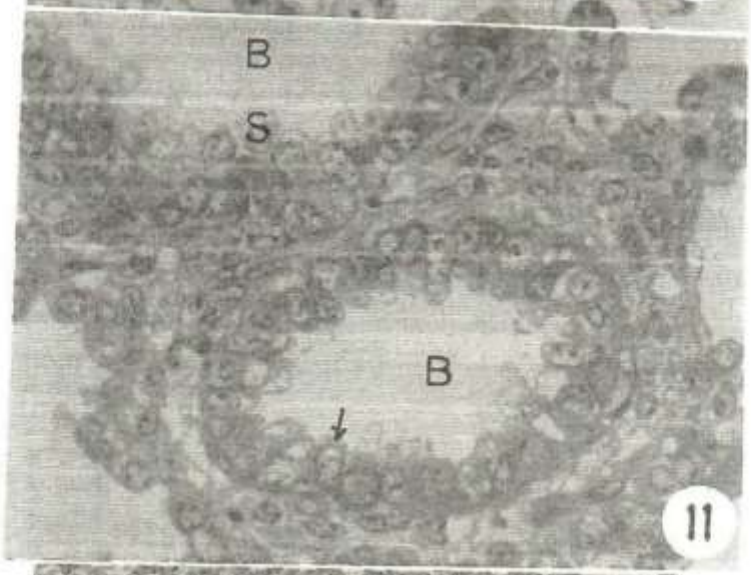
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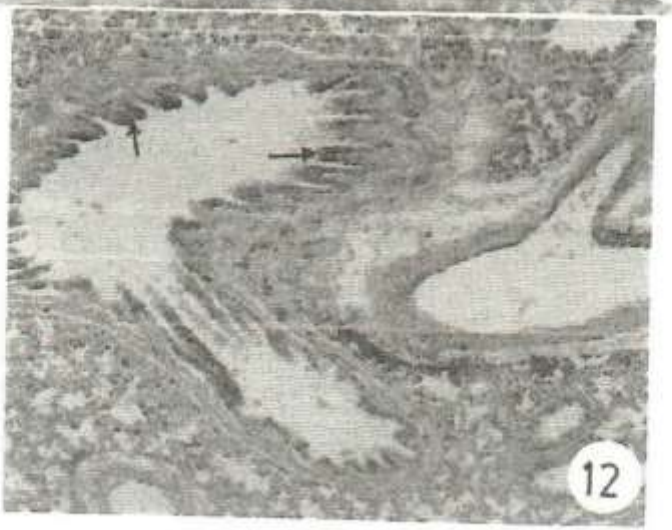
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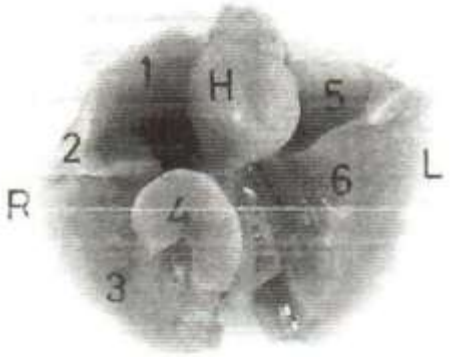

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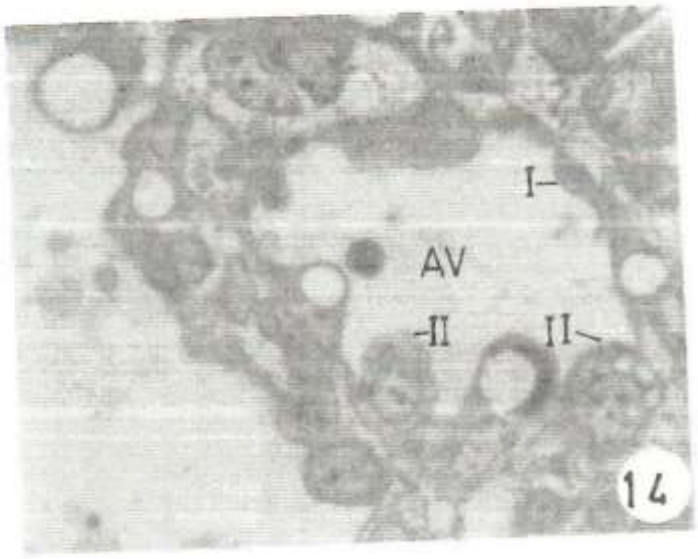

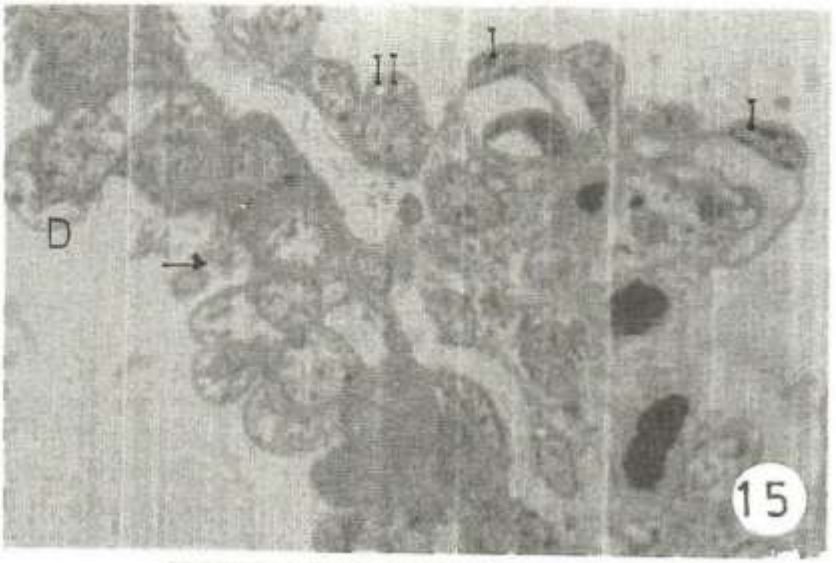
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I
D
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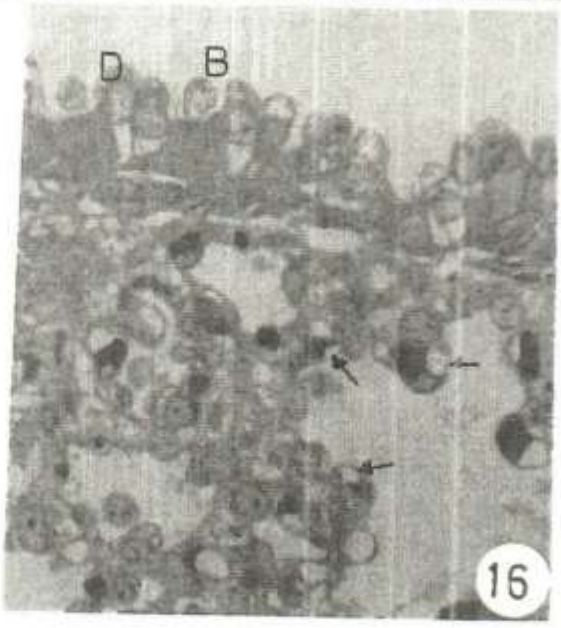
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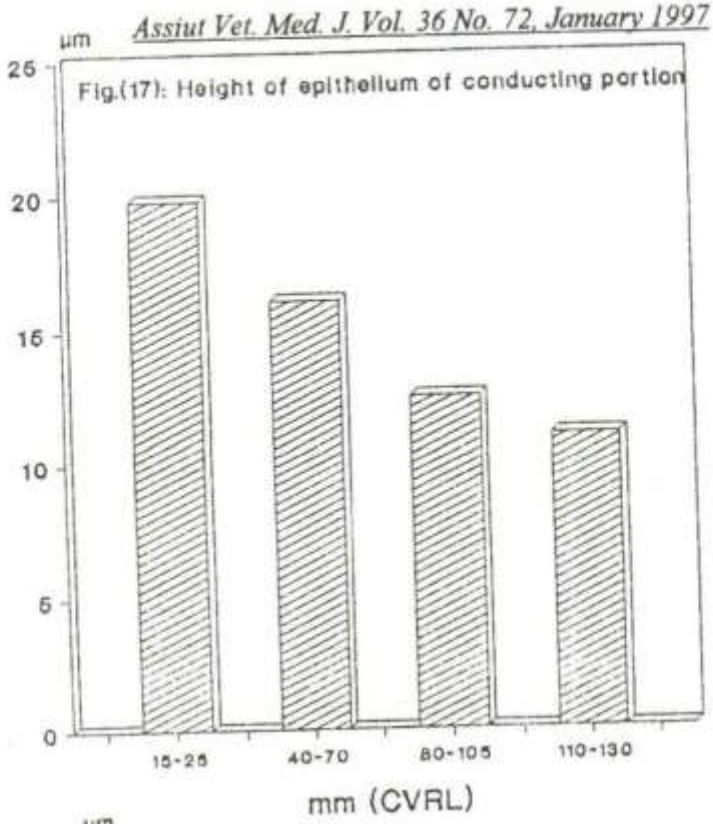

Fig.(17): Height of epithelium of conducting portion

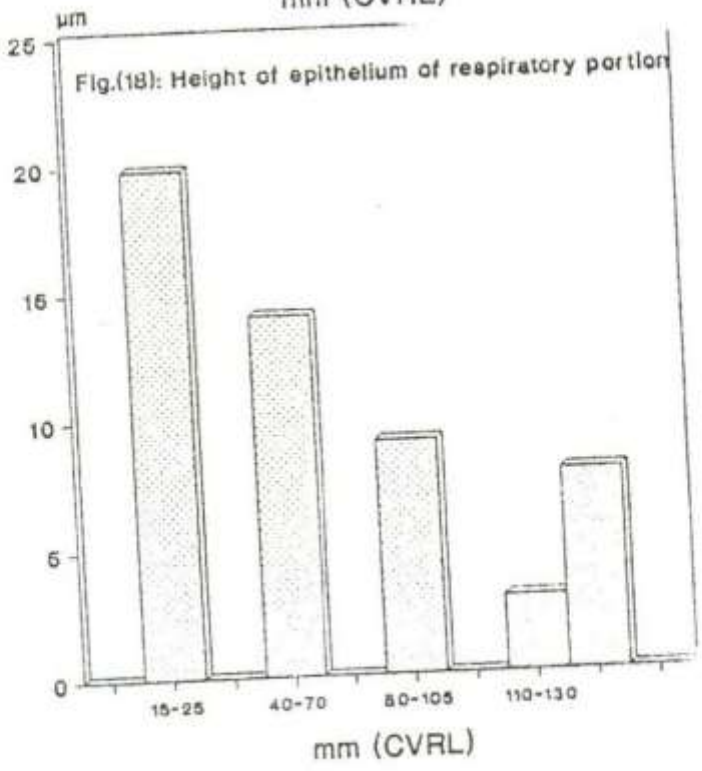

Fig.(18): Height of epithelium of respiratory portion