# Lecture1 of organopathology د.ابتسام جواد علي

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## Avian Respiratory System

The avian respiratory system is involved in the following functions:absorption of oxygen (O2),release of carbon dioxide (CO2),release of heat (temperature regulation),detoxification of certain chemicals rapid adjustments of acid/base balance and vocalization .

## Parts of the Chicken Respiratory System

nasal openings , nasal cavities , the pharyngeal region of the mouth. The cranial larynx (sometimes referred to as the superior larynx or glottis), located in this pharyngeal region, is the opening to the trachea. After air passes through the cranial larynx, it continues through the trachea. The trachea is made up of cartilaginous rings that keep it from collapsing due to the negative pressure present when a chicken breathes in air. The syrinx (or caudal larynx), located near the end of the trachea, is the chicken's voice box. A chicken does not have vocal cords to produce sound. Instead, a chicken's "voice" is produced by air pressure on a valve and modified by muscle tension..After the syrinx, the trachea divides into two much narrower tubes called bronchi. In some respiratory diseases, tracheal plugs form and physically block the respiratory tract at the junction of the bronchi, thus suffocating the chicken.

Each bronchus (singular of bronchi) enters a lung.Chicken lungs are relatively small, are firmly attached to the ribs, and do not expand. Birds have an incomplete diaphragm and chest muscles and a sternum (keel) that do not lend themselves to expansion in the way that amammal's chest muscles and sternum do. Consequently, abird's lungs operate differently from those of a mammal.Mammalian lungs contain many bronchi that lead to small sacs called alveoli. Because an alveolus (singular of alveoli) has only one opening, air flows into and out of the alveolus but not through it to the outside of the lung. In comparison, air passes through a bird's lungs in one direction. (In fact, the mammalian respiratory system is described as tidal because air goes in and out like the tide, whereas the avian respiratory system is described as non tidal. A bird's lungs contain parabronchi, which are continuous tubes that allow air to pass through the lung in one direction, and airsacs. The parabronchi are laced with blood capillaries, and it is here that gas exchange occurs. The air sacs, which fill a large proportion of the chest and abdominal cavity of a bird, are balloon-like structures at the ends of the airway system.

The key to the avian respiratory system is that air moves in and out through distention and compression of the air sacs, not the lungs. The air sacs act as bellows to suck air in and blow it out and to hold part of the total air volume. At any given moment, air may be flowing into and out of the lung and being "parked" in the air sacs.Air sacs are some what unique to avian species, found else where only in certain reptiles. In the chicken, there are nine such sacs: an unpaired one in the cervical area, two interclavicular air sacs, two abdominal air sacs, two anterior thoracic air sacs, and two posterior thoracic air sacs. Another important feature of the avian respiratory system is also part of the avian skeletal system.Some of a bird's bones are hollow. The air sacs in a bird's lungs connect to the air spaces in these bones, and the bones then act as part of the avian respiratory system. They are called pneumatic bones and include the skull, humerus, clavicle, keel, pelvic girdle, and lumbar and sacral vertebrae. Abroken pneumatic bone can cause a bird to have difficulty breathing.

**Anatomy and Histology**

The respiratory system begins at the nares and includes the nasal chamber, larynx, trachea, syrinx, lungs, air sacs, and associated sinuses and glands. The nasal chamber contains cartilaginous turbinates (conchae) that provide support and divide the chamber into rostral , middle, and caudal compartments.The rostral nasal chamber is lined by squamous epithelium having a distinctive scalloped surface resembling the pattern of a tile roof. The middle nasal chamber is lined by pseudostratified columnar ciliated epithelium. Variable numbers of lymphocytes and numerous intraepithelial mucous glands containing goblet cells are in the lamina propria.
The caudal nasal chamber begins with a respiratory epithelial lining that changes to specialized olfactory epithelium comprised of basal cells, supporting cells, and sensory cells. This arrangement of turbinates and chambers increases the respiratory surface area and facilitates the critical filtering function as well as providing for temperature and humidity modifications that occur as air moves from the envtronment into the gas exchange system in the lungs. Nasal (salt) glands and their ducts are located lateral to the nasal cavity. Large nasolacrimal ducts drain secretions of the Harderian and lacrimal glands.Paired infraorbital sinuses are located ventral and anterior to the orbit, occupy a large area in the head, and are lined by squamous or low to medium ciliated columnar epithelium with a few simple mucous glands. The number of glands and amount of ciliated epithelium increases

near
the entrance of the sinus into the nasal cavity. Communication of infraorbital sinuses with the nasal cavity is located caudally and dorsally, thus the sinuses discharge onto the ventral position of the olfactory epithelium in the caudal nasal chamber. This anatomical arrangement makes drainage from the infraorbital sinus difficult, and explains the swelling of the sinus that is common in sinusitis associated with many respiratory infections. The choanal cleft in the floor of the nasal chamber provides direct communication between the nasal and oral cavities and forms the oropharyngeal region. The larynx is lined by cuboidal to columnar ciliated epithelial cells. The trachea is lined by ciliated pseudostratified columnar epithelium similar to that found in the middle and posterior nasal chambers. The lamina propria of the normal tracheal mucosa is relatively thin and contains large numbers of simple alveolar mucous glands. Goblet cells are more prominent in the distal portions of the trachea. The ciliated epithelium, mucus, and mucous secreting cells in the respiratory tract comprise the mucociliary blanket which constitutes an essential mechanism for entrapment and clearance of particulate material from the respiratory tract.. Cartilaginous rings that are complete and overlap with adjacent ones support the trachea. The avian lung has a characteristic structure that is very different from that of mammals. which are covered by pleura ,Primary bronchi are lined by pseudostratified columnar ciliated epithelium, with variable numbers of mucous glands and focal areas of lymphoid tissue in the lamina propria. Secondary bronchi that arise from primary bronchi also are lined by similar epithelium but have few or no cartilaginous rings.Parabronchi, also termed tertiary bronchi, arise from secondary bronchi and form the core of the hexagonal respiratory units or lobules where gas exchange occurs in the surrounding air-blood capillary bed.Air flows from parabronchi into atria that open off the parabronchus. Atria are separated from each other by interatrial septa. Septa are composed of fibro vascular connective tissue and have smooth muscle ontheir surface. By contracting and relaxing, smooth muscle controls airflow into the atria. Macrophages are often found in the inter stitiutn at the base of septa. Air from atria flows into infundibula that extend off of the atria and connect with air capillaries where gas exchange occurs. Respiratory lobules consisting of a parabronchus, atria, infundibula, and air-blood capillary bed are separated by thin interstitial tissue that contains blood vessels, nerves, and occasionally

small parasympathetic ganglia.Parabronchi are lined by a simple cuboidal to squamous epithelium that continues into the atria and infundibula. Air capillaries are lined by simple squamous epithelium. Epithelial cells lining atria and infundibula respond quickly to injury by becoming hypertrophic,
hyperplastic, and, in some cases, resulting in the generation of numerous phagocytic cells. This pattern is a proliferative response in contrast to an exudative response characterized by fibrin, heterophils, histiocytes (macrophages), and lymphoid cells. Exudative and proliferative responses often occur together. Air sacs originate from the ends of primary and some secondary bronchi. Small air saccules extend from parabronchi on the surface of the lung. Air sacs are lined by simple squamous epithelium,but there are scattered patches, also called tracts, of ciliated columnar epithelium that are more numerous at the openings (ostia) of the
air sacs from the bronchi. Tracts of mucociliary epithelium extend from the ostia caudally but they are difficult to appreciate in routine histologic sections. These patches or tracts of respiratory epithelium provide sites for attachment of organisms, *e.g.*, mycoplasma.The number of air sacs varies from 7 to 9 among avian species.The cervical, clavicular, and cranial thoracic air sacs are grouped together as the cranial air sacs. The caudal thoracic and abdominal air sacs are grouped together as the

caudal air sacs. This grouping is important because air entering the cranial air sacs is filtered by passing through portions of the lung, whereas air entering the caudal air sacs does not have this filtration step. This makes caudal air sacs more likely to be sites of infections. Air sacs extend into the
pneumonic bones, and air sac infection can extend into these bones, resulting in osteomyelitis. Air sacs serve as a bellows system to move air through the fixed lungs. Air moves in a unidirectional pattern through the lung - caudal to cranial - with the air flowing in a countercurrent direction to the flow of blood in the blood capillary network. This large and efficient gas-blood exchange surface results in increased susceptibility to inhaled toxic substances. Practical application of this fact was the earlier use of canaries for detection of toxic gases in mines.

**1-Responses to Injury**

Histologic evidence of injury to the respiratory epithelium includes

1-loss of cilia (deciliation), swelling and hydropic vacuolation of cells, desquamation, necrosis, hyperplasia, and metaplasia.
2-Mucous glands may be hypertrophic or hyperplastic or may show loss (depletion) of mucus, necrosis, or atrophy.

3-Inflammatory lesions are primarily characterized by hyperemia, deposition of fibrin ,and infiltration of inflammatory cells that include heterophils, lymphocytes, macrophages, and plasma cells.

4-Hemorrhage may occur,but care must be exercised in interpreting the presence of blood inairways of the trachea, bronchi, and parabronchi, as blood readily flows through tears in the air sacs during postmortem examination,and is a common artifact.

5-Epithelial cell hyperplasia, particularly evident in trachea ,but also seen in primary and secondary bronchi, can result in 5-6 layers of undifferentiated cells that later may differentiate into ciliated cells and mucous gland cells.

This lesion indicates the regenerative or repair phase following injury to the respiratory mucosa. Regeneration of the epithelium occurs rapidly, beginning within 48 hours. Increased numbers of lymphocytes, macrophages, and plasma cells in the lamina propria are frequently found in the reparative/regenerative phase.Lymphoid cells may aggregate to form lymphoid nodules, some with germinal centers.

Basic responses of the respiratory system to injury can be initiated by environmental insults *e.g.*,

excess ammonia and dust, spray administration of live vaccines, infection with respiratory viruses,bacteria, fungi, parasites, *etc*. Environmental insults and respiratoty viruses (including viruses in live vaccines) frequently result in damage to the defense mechanisms of the respiratory system leading to bacterial infections.

some lesions in the respiratoty system are specific,*e.g.* , intranuclear inclusion bodies in syncytial epithelial cells in infectious laryngotracheitis or presence of identifiable infectious and parasitic agents, most lesions are not disease specific. The patterns of injury and response provide guidelines as to possible etiology.For example, the transition between squamous epithelium lining the anterior nasal chamber and respiratory epithelium lining the middle nasal chamber is a common site for squamous metaplasia that occurs in vitamin A and some B-vitamin deficiencies.

**1-Non-Infectious Condition sikhnn**

Mechanical injury to the nasal chamber and associated turbinates can be caused by trauma that may occur in the beak trimming process or during placement of chicks or poults. Lesions include necrosis with loss of epithelium, inflammation, and, in some cases,necrosis of the underlying turbinate cartilage. Colonies of bacteria may be seen in the necrotic tissue. Plant material may be found in the nasal chambers and is associated with increased amounts of mucus, inflammation, necrosis, and regeneration of epithelium. This foreign material likely originates from the litter.

Inhalation of ammonia, dust, or other noxious gases can cause lesions and most often makes the respiratory system more susceptible to infection, especially bacterial infection. Alterations in the morphology of cilia or loss of cilia, attenuation of the mucosa epithelium, mucosa gland and goblet cell hypersecretion and hyperplasia, and accumulation of excess mucus in the lumen of airways occurs in response to ammonia exposure. In the lungs, dust material may be found free or within macrophages adjacent to parabronchi and atria and may not be associated with any other responses. A modest histiocytic response may occur.Lymphocytes may indicate an inunune response to antigenic material in the dust, such as feather dander. Dust material usually appearsas irregular, retractile, brown particles that are often variably bifrefringent with polarized light. Carbon particles produce a similar

tissue response but are black and relatively uniform. They typically result from smoke inhalation including second-hand tobacco smoke. Urates retained because of renal failure may become deposited in vessel walls, and in the capillary network of the respiratory lobules. Necrosis, heterophilic and histiocytic infiltration, and the typical feathery, starburst pattern left by the urate crystals, which dissolve in aqueous solutions during tissue processing, are seen. Diffuse deposition of mineral along basement membranes (metastatic mineralization) in the lungs may occur in chronic renal failure.Toxic gas injury is exemplified by polytetrafluoroethylene(PTFE) released when Teflon® coated surfaces are over heated.This injury is characterized by accumulation of protein rich fluid including fibrin in bronchi, especially in parabronchi and

secondary
bronchi. Pneumocytes become hyperplastic frequently resulting in accumulation of large numbers of macrophages. Exogenous lipid pneumonia has many of the same features with accumulation of lipid in the cytoplasm of macrophages and/or proliferation of adipose cells within lobules.

**2- *Viral infections***

Infectious bronchitis virus, avian influenza virus, certain types of avian paramyxoviruses (including Newcastle disease), metapneumovirus, poxvirus, adenovirus, and laryngotracheitis virus are important viral pathogens of the avian respiratory system. Viral infections may result in minimal and transito1y lesions unless complicated by environmental factors and/or secondary bacterial infections. Initial damage and impairment of the respiratory defense mechanism frequently lead to complications caused by a secondar1y bacterial invaders, *e.g.* , *E. coli.* Adenoviruses produce large, irregular, basophilic, intranuclear inclusions in respiratory epithelial cells with minimal, if any, inflammatory response in turkeys. Quail bronchitis is an adenoviral infection that causes severe damage and inflammation of the tracheal mucosa. There may be similar necrotizing and proliferative lesions in the epithelia of the nasal mucosa, prima1y and seconda1y bronchi, nasal passages, and air sacs. Air sacs often contain necrotic debris and have regions of epithelial hyperplasia associated with increased thickness of the airsac wall. Multifocal necrosis with intranuclear inclusion bodies also may be found in visceral organs, especially liver. Infectious laryngotracheitis, a herpes virus infection of chickens, causes extensive necrosis of epithelial cells, frequently with hemorrhage. Necrosis leads to regenerative hyperplasia of the epithelium in birds that survive the initial acute phase of infection. Intranuclear inclusions in individual cells and in characteristic large syncytial epithelial cells may be found in conjunctiva! epithelium, epithelium of the middle nasal chambers and infraorbital sinuses, tracheal epithelium, and/or in bronchial epithelium, especially at the junction with air sacs, and in air sacs. Syncytial

cells with intranuclear inclusions also may be present in the mucosa of the upper alimentary tract. Typically a single large, finely granular, basophilic inclusion body fills the entire nucleus, but inclusions can be small, eosinophilic, and surrounded by a halo. Margination of nuclear cluomatin is often prominent. Marked heterophilic infiltrates and intraluminal fibrinoheterophilic exudates are common in the early, acute phases of infection. Examination of exudate in the tracheal lumen may reveal single cells or syncytial cells with inclusion bodies when none can be found in the mucosa. Areas of epithelium that are not necrotic show loss of cilia and increased mucous production. Lymphoid cell infiltrates in the lamina propria of the tracheal mucosa are a common response if affected chickens survive several days.
Avian influenza, infectious bronchitis, and infection with certain avian paramyxoviruses, especially avian paramyxovirus type 1 (Newcastle disease virus), cause similar lesions in the respirato1y system and thus diagnosis of a specific viral etiology cannot be made by histopathology alone. Loss of cilia and swelling, hydropic degeneration, and necrosis of epithelial cells are followed by epithelial regeneration, in which multiple layers of regenerating, undifferentiated epithelial cells line the mucosa. The associated inflammatory response results in edema, and heterophilic and lymphocytic infiltrate in the lamina propria. Heterophils, especially those in the luminal exudate, usually degranulate, and become difficult to recognize. Mucous gland hyperatrophy and hyperplasia are frequent. The trachea is a primary target site for both avian paramyxovirus type 1 and infectious bronchitis virus. Influenza virus is likely to cause lesions in lungs and sinus, in addition to the trachea. Infectious bronchitis tends to cause necrosis of widely scattered individual epithelial cells that may be phagocytized by macrophages resulting in a pattern of hyperplastic epithelium containing vacuoles. Increased thickness of the tracheal mucosa due to epithelial hyperplasia and/or increased numbers of lymphoid cells in the lamina propria are characteristic lesions of infectious bronchitis and avian paramyxovirus type 1 infections; however, it is important to emphasize that those lesions are not diagnostic for either disease.
The diphtheritic form of avian pox is characterized by hyperplasia and ballooning degeneration of epithelial cells, with the presence of large, eosinophilic, intracytoplasmic inclusion bodies in

infected cells. Epithelial hyperplasia frequently results in prominent projections of cells into the tracheal lumen.

***3-Bacterial infections***

*Bordetella avium, Avibacterium paragallinanarum* (formerly *Haemophil11s paragallinarnarum), Ornithobaclerim rhinotracheale* (ORT), *Pasturella multocida, E. coli, Staphylococcus* spp., *Riemerella analipestife,; Gallibacterium analis, Mycobac/erium* spp. , other less frequently occurring bacteria, mycoplasmas *(Mycoplasma gallisepticum, M. synoviae, M. meleagridi;),* and *Chlamydia psittaci* are bacterial agents that share many common tissue responses to injury, yet have some distinctive features that aid in their identification.

1-**The infraorbital sinus** is a primary site of infection with *Avibaclerium paragallinarm;* a characteristic feature is the presence of numerous bacteria associated with cilia.

2-The trachea is a primary site of infection with *Bordetela avium*, with bacteria characteristically closely associated with cilia of the mucosa[ epithelium in acute infections. Degenerative lesions (loss of basophilia) in the tracheal cartilage may be present in chronic cases of bordetellosis and lead to marked deformity of the trachea l rings. Hyperplastic bronchial-associated lymphoid tissue in the lung is another feature of avian bordetellosis.
*3-Pasleurella multocida,* ORT, *E. coli,* and staphylococci produce major lesions in the lungs. Lesions caused by *P multocida* and ORT are characterized by large areas of necrosis with edema and accumulation of fibrin and heterophils in interstitial tissues, capillary beds, and bronchi. Necrotic areas often contain visible basophilic bacterial colonies. In *E. coli* pneumonia, necrosis also is a prominent feature , but lesions are usually centered on parabronchi with less involvement of the capillary bed and interstitial tissues. Bacterial colonies are usually visible in exudate and necrotic areas. Characteristic coliform colonies are composed of bacilli, are round with a thin densely stained margin , and have irregular lack of staining centrally. In acute infections in young or immunosuppressed birds, macrophages with large numbers of intracytoplasmic bacteria may be seen. Epithelium of primary and secondary bronchi is likely to have loss of cilia and show degenerative, necrotic, and hyperplastic changes. Activated epithelial

cells of the atria and infundibula become hypertrophic,hyperplastic, and result in an increased cellularity within affected parabronchi. Heterophils usually are numerous. Parabronchial casts composed of caseous exudate containing typical colonies are characteristic of coli form pneumonia. A thick layer of fibrinoheterophilic exudate may be present on the pleural surface (pleuritis).

Air sacs are common lesion sites in respiratory colibacillosis, with epithelial cell necrosis and regeneration, edema, fibrin,heterophils, and lymphoid cells accumulating that increase the thickness of the affected air sacs.

*Staphylococcus* may produce multifocal granulomatous lesions that resemble mycotic infections both grossly and microscopically. However, intra lesional botryoid colonies composed of gram-positive cocci readily di stinguishes staphylococcal lesions from those produced by fungi

Infection with *Mycobacterium* can result in multiple histiocytic granulomas in the lungs. They usually have a central area of caseous necrosis surrounded by large macrophages (epithelioid cells)and multinucleated giant cells, or they may be composed only of aggregates of primarily large macrophages. ln either case, macrophages in the granulomas usually have abundant cytoplasm with a finely granular appearance. An acid-fast stain reveals numerous acid-fast bacilli in the cytoplasm of few or many macrophages. Similar lesions are likely in the digestive tract and may also be found in other organs including the skin.Chlamydiosis caused by *Chlamydia psitaci* often causes infiltration of lymphoid cells in parabronchi and interstitial tissue, accompanied by hyperplasia of epithelial cells in atria and infundibula.Airsacculitis, characterized by the presence of fibrin , heterophils, and lymphoid cells, with epithelial cell hyperplasia, is common in chlamydiosis. lntracytoplasmic colonies of the organism appear as cytoplasmic basophilic smudges, but are not common and difficult to definitively identify. Lymphocytic tracheitis and sinusitis and mucus gland hyperplasia in sinuses are characteristic lesions of *M. gallisepticum* infection in chickens and turkeys, but they are not diagnostic. Presence of many lymphocytes in diffuse and nodular collections (lymphofollicular reaction), in lungs and air sacs is suggestive of mycoplasmal infection. Marked hyperplasia of bronchial-associated lymphoid tissue in lungs should arouse suspicion of mycoplasmal infection. Acute inflammation, characterized by fibrin and infiltration of large numbers of

heterophils with few, if any, lymphocytes, is prominent in the early stages of mycoplasmal infections. Epithelial regeneration following initial damage by mycoplasma is common.

## *Fungal infections*

Mycotic infections of the respiratory system are common. *Aspergillus* spp. is the fungi most frequently infecting turkeys and chickens. Lesions caused by fungi are most common in the lungs and air sacs but they may also be found in trachea (mycotic tracheitis). Mycotic granulomatus usualy occur as multiple, variably sized areas of caseous necrosis surrounded by macrophages and multinucleated giant cells. Non-caseous granulomas consisting of histiocytes and multinucleated giant cells are also a histologic feature of mycotic infection. In some granulomas, fungal hyphae are present within the necrotic areas. Visualization of fungal hyphae, enhanced by special stains such as periodic acid Schiff (PAS) or Gomori's methenamine silver (GMS), is diagnostic. lesions vary in size from pinhead or miller seed (milliary <1 mm in diameter) white to yellowish granulomas up to the size of a pea. Roughly spherical granulomatous nodules (>2 cm) may also be observed in serosa and parenchyma of the other organs involved .Pulmonary lesions are characterized by multiple hard creams to yellow colored, circumscribe plaques a few mm to several cm in diameter seen throughout the lungs surface, inside the lungs, scattered in ventral surface of sternum and air passages on gross examination . The plaques also found in the syrinx, air sacs, debilitating, voice change or exercise intolerance .Granulomatous nodules and /or cheesy plaques on the serosa and parenchyma of respiratory tracts as well as other organs are observed.

## Parasitic infections

Cryptosporidiosis is an example of a protozoan disease that causes loss of cilia and pronounced hyperplasia of epithelial cells. Cryptosporidia are round to ovoid, basophilic bodies,about 4-6 pm in diameter, and are intimately associated with the surface of mucosa! epithelium. In pet birds infected with the protozoan *Sarcocystis falcatula,* there is interstitial pneumonia and areas of necrosis and fibrin deposition in the lung. Oval or long,sinuous meronts are found in the vascular endothelium of blood capillaries in the capillary bed. Gametocytes of *leucocytozoon,* and meronts of *Plasl/lodiu//1, Haemoproteus,* and *leucocytozoon* may be

found
in the lung where they plug blood capillaries. Presence of protozoan parasites in the lungs is suspected when the pattern of erythrocytes in the air capillaries is altered with the erythrocytes not being "lined up" to pass through the blood capillaries in the usual pattern. The nematode *Syngamus trachea* can cause epithelial cell hyperplasia and loss of cilia with increased thickness of tracheal mucosa due to lymphoid cell infiltration.

**Neoplasia**

Although relatively uncommon in poultry, primary or metastatic tumors may occur in the respiratory system, particularly in the lung. Primary tumors are reported as arising from respiratory epithelium of primary or secondary bronchi, and from air sac epithelium. Adenocarcinomas, including those of reproductive tract origin, may metastasize to the lung. Squamous cell carcinomas and melanosarcomas are described in the lung. Lymphoid tumors of Marek's disease are the most common tumors found in the lungs of chickens.