INTERSTITIEL PNEUMONIA

Localization of Inflammation

The inflammation is localized in the:
Interalveolar (between alveoli),
Interlobular (between lobules),
Peribronchial, and
Perivascular regions.
Therefore, the **alveolar spaces are usually empty**, and the **main inflammatory reaction** is observed in the **connective tissue and around blood vessels.**

ETIOLOGY

Viral, Allergic, and Parasitic Agents

The **majority of interstitial pneumonias** belong to this group.

Occasionally, **Mycoplasma** and **Chlamydia** strains can produce a similar pathological picture.

It often occurs **secondary to other pneumonias**, for example:

- **Distemper** (in dogs)
- **Bordetella bronchiseptica** infections
- Following **catarrhal bronchopneumonia**

ACUTE INTERSTITIAL PNEUMONIA

Infectious Agents:

- *Distemper*, *Feline Infectious Peritonitis (FIP)*
- *Salmonellosis* in calves or pigs
- *Toxoplasmosis*
- *Lungworms* and *Ascarid larval invasions*

Inhaled Gases:

- Excessive oxygen (**>50% O_2**)
- Cigarette smoke
- Chemical gases

Alimentary Toxins:

- **L-tryptophan** and certain **drugs**

Endogenous Toxins:

- **Endotoxic shock**, **uremia**, **pancreatitis**

Allergic Reactions (Hypersensitivity):

- For example, **"allergic pneumonia."**

CHRONİC INTERSTİTİAL PNEUMONİA

Inhaled Dusts (Pneumoconioses):

- **Silica**, **coal dust**, and similar particulates.

Infectious Agents:

- **Ovine Progressive Pneumonia (Maedi)** in sheep
- **Chronic African Swine Fever**
- **Tuberculosis** (outside primary lesions)
- **Histoplasmosis**
- **Parasitic verminous pneumonias**

Ingested Toxins:

- **Pyrrolizidine alkaloids** (in horses, pigs, calves, and sheep)

Allergic Causes:

- **Hypersensitivity reaction** to *Dirofilaria immitis* microfilariae in dogs

Radiation:

- Can be induced experimentally in **laboratory animals** and **dogs**

Collagen–Vascular Disorders:

- e.g., **Canine Systemic Lupus Erythematosus (SLE)**

MACROSCOPİC (NECROPSY) FİNDİNGS

- Lesions may be **so mild** that they can be **easily overlooked**.
- Generally, there is **no marked consolidation** (solidification) of the lung tissue.
- Upon opening the thoracic cavity, the **lungs fail to collapse properly**.
- **Widespread emphysema** is frequently observed.
- **Color:**
- **Dark red** → if **hyperemia** predominates
- **Pale** → if **interstitial pressure** and **emphysema** compress blood vessels
- **Consistency:**
- **Normal** or **spongy/crepitant** in emphysematous cases
- **Cut Surface:**
- **Dry**, with **no exudate oozing**, and **bronchi appear empty**.

- **In Chronic Cases:**
- **Peribronchitis nodosa** develops → the **bronchial walls thicken**, and **bronchioles** appear as **pinpoint-sized nodules**.
- **In Acute Cases:**
- Due to **peribronchial cellular infiltration**, the **bronchial walls** appear **thickened**.

HISTOPATHOLOGICAL FINDINGS

- **A. Acute Stage**
- Inflammation is concentrated in the **alveolar walls**, **interlobular**, **peribronchial**, and **perivascular** regions.
- **Mononuclear cell infiltration** predominates, consisting of **lymphocytes**, **plasma cells**, **histiocytes**, or **monocytes**.
- **Neutrophils are few**, which distinguishes it from **bacterial pneumonia**.
- In **allergic cases**, **eosinophils** may also be present.
- **Type II pneumocytes** proliferate and take on a **cuboidal shape**, producing an appearance referred to as:
  - **"Epithelialization"**, or
  - **"Fetalization"** (resembling **fetal lung structure**).
- A **hyaline membrane** may form on the **alveolar surface**.

- **B. Chronic Stage**
- **Proliferation** of **interalveolar** and **interlobular connective tissue** is prominent.
- **Lymphocytes** and **histiocytes** are densely accumulated.
- **Alveolar** and **bronchial epithelium** show **hyperplasia**.
- **Alveoli** may appear **gland-like** in structure.
- **Interstitial areas** contain **plasma cell** and **lymphocyte aggregates**, with **increased collagen fibers**.
- **Hyperplasia** of **terminal bronchial smooth muscles** leads to **peribronchitis nodosa**.
- **Expansion** of **interlobular connective tissue** further **aggravates emphysema**.

OUTCOMES

•**Complete Recovery:**
•Through **epithelial regeneration** and **resolution of inflammation**.
•**Fibrosis and Structural Remodeling:**
•Healing by **fibrosis** leads to **thickened interalveolar septa** and **reduced elasticity**.
•**Secondary Complications:**
•Development of **catarrhal, fibrinous,** or **necrotic pneumonia** following secondary infection.
•**Chronic Sequelae:**
•**Chronic bronchitis**, **bronchiolitis**, and **emphysema** may persist due to irreversible tissue changes.

DISEASES ACCOMPANIED BY INTERSTITIAL PNEUMONIA

VIRAL INTERSTITIAL PNEUMONIA

•Viral pneumonia is common in **young animals**, especially in **autumn and winter**.
•The disease is **multifactorial**; it is influenced by **viral infections**, environmental stress, and **secondary bacterial infections**.

VIRAL INTERSTITIAL PNEUMONIA

Main viral agents:

- Parainfluenza-3 (PI-3)
- Adenoviruses
- Reoviruses
- Respiratory Syncytial Virus (RSV)
- Infectious Bovine Rhinotracheitis (IBR) virus
- Mucosal Disease virus

•**Secondary bacterial agents:** *Corynebacterium pyogenes, Pasteurella spp., Chlamydia sp., Hemophilus sp., Streptococcus sp., Staphylococcus spp., Pseudomonas aeruginosa,* etc.
•Secondary infections can transform interstitial pneumonia into **purulent**, **abscess**, or **fibrinous** pneumonia.
•When combined with intestinal infection, it may cause **lung–bowel syndrome**, leading to diarrhea.

MYXOVİRUS INFECTİONS (INFLUENZA GROUP)

•Usually cause **catarrhal infection** of the **upper respiratory tract**.
•Pneumonia develops **secondarily**.

Pig Influenza
•Caused by **Influenza Virus Type A (Myxovirus)**.
•**Highly contagious**; may affect the entire herd at once.
•Often associated with **verminous pneumonia**.
•**Seasonal**, especially during cold months.
•**Secondary bacterial infections** (Hemophilus, Pasteurella) are common.
•When the virus spreads to the lungs, **interstitial pneumonia** appears, mainly in the **anterior lobes**.

EQUİNE INFLUENZA

- Caused by **Orthomyxovirus (Influenza A, equi virus type I)**.
- Primarily affects the **upper respiratory tract**, causing **hyperemia**, **bronchitis**, and **broncho-interstitial pneumonia**.
- Lesions show **edema, desquamation**, and **focal erosions**.
- If secondary bacterial infection occurs (*Streptococcus, Staphylococcus, E. coli*), abscesses and severe pneumonia may develop.
- In chronic cases, **peribronchitis nodosa** forms and contributes to **"fading of horses"**.

BOVİNE PARAİNFLUENZA-3 (PI-3) INFECTİON

- Causes **inflammation** of the **upper respiratory tract** with **mucous nasal discharge**.
- May appear as a **pure (primary)** infection or combine with other pathogens in **Shipping Fever** and **Enzootic Pneumonia**.
- Lesions are typically found in the **cranioventral** regions of the lungs.
- Lesion type: **broncho-interstitial pneumonia** with **atelectasis**.

Microscopy:

- Hyperplasia of bronchial epithelium (2–4 days after infection).
- **Intracytoplasmic inclusion bodies** → diagnostic feature.

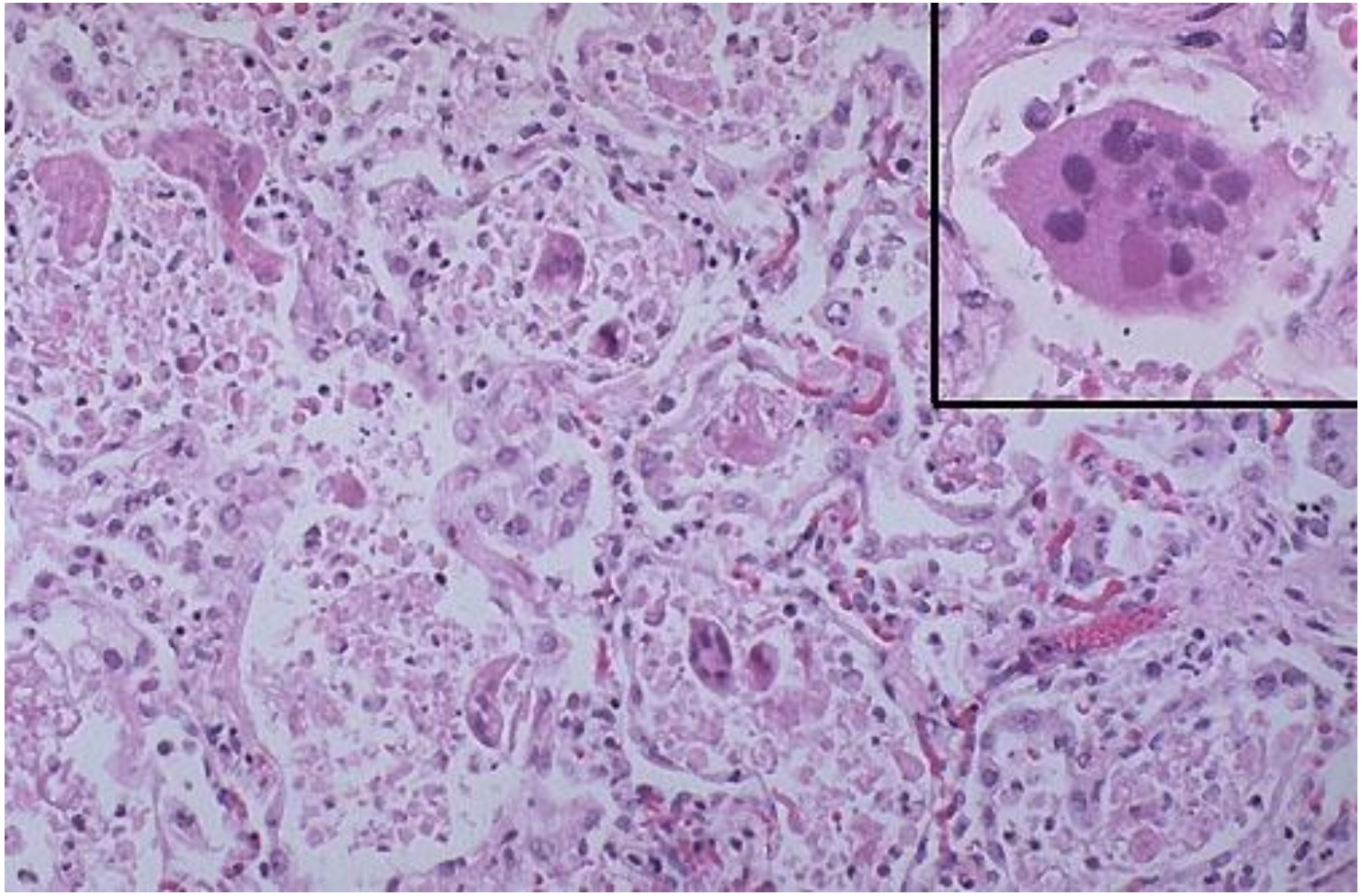
BOVİNE RESPİRATORY SYNCYTİAL VİRUS (RSV) INFECTİON

•Caused by **Pneumovirus** (family *Paramyxoviridae*).
•Very common; most herds have antibodies.
•Often part of **bovine flu complex**.

Macroscopic:
•Lesions are usually mild.
•Degenerative rhinitis, catarrhal bronchitis, bronchiolitis, swollen lymph nodes.
•Lung lesions localized in **cranioventral** regions.
•**Atelectasis** and **interstitial or bullous emphysema** in caudal parts.

BOVİNE RESPİRATORY SYNCYTİAL VİRUS (RSV) INFECTİON

- **Microscopic:**
- Acute bronchitis and bronchiolitis.
- Epithelial proliferation → **multinucleated syncytial cells**.
- **Intracytoplasmic inclusion bodies** in epithelial cells.
- These two findings are **pathognomonic** (diagnostic).
- Also, interstitial pneumonia, atelectasis, emphysema, and hyperplasia of peribronchial lymph follicles.



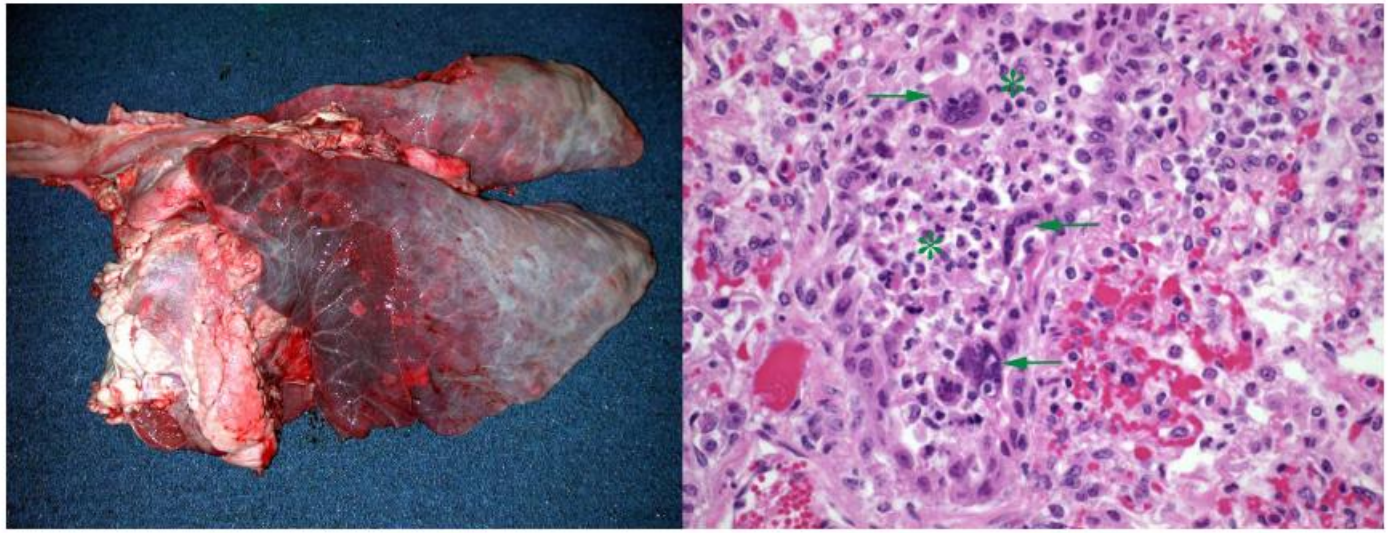


Figure: Bovine respiratory syncytial virus. ***Left:*** *The cranioventral lung is reddened and collapsed, but the rubbery texture helps to distinguish this from a bronchopneumonia.* ***Right:*** *A bronchiole contains necrotic cells in the lumen (*), and multinucleated epithelial syncytia in the lining epithelium (arrows). These syncytia are diagnostic, but they are only present in the first 1-4 days of clinical illness.*

https://ecampusontario.pressbooks.pub/pathologyoftherespiratorysystem/chapter/respiratory-diseases-of-cattle/

CANİNE DİSTEMPER

•Caused by **Morbillivirus** (family *Paramyxoviridae*).
•Affects many organs (pantropic virus).
•Infection starts in **lymphoid tissues** (lymph nodes, tonsils).
•If neutralizing antibodies develop within 8–9 days, virus spread stops.
•Mostly affects **young dogs (<1 year)**; in older dogs, causes **Old Dog Encephalitis**.

- **Clinical Forms:**
- **Respiratory form:**
  - Interstitial pneumonia (primary).
  - Secondary infection with *Bordetella bronchiseptica* → catarrhal or purulent bronchopneumonia.
- **Digestive form:**
  - Catarrhal or hemorrhagic gastroenteritis.
- **Nervous form:**
  - Non-purulent encephalitis or encephalomyelitis (especially in older dogs).
- **Ocular form:**
  - Conjunctivitis, keratitis.
- **Cutaneous form:**
  - Eczema-like lesions, hyperkeratosis (“hard pad disease”).

- **Diagnosis:**
- Presence of **intranuclear and intracytoplasmic inclusion bodies** in neurons, glial, and epithelial cells.
- **Demyelination** and **non-suppurative encephalitis** are characteristic.

In dogs distemper disease occurs primary interstitial pneumonia due to virus!

This table changes by secondary addition of bacteria such as Bordetella bronchiseptica. Catarrhal or other bronchopneumonia are formed!

PESTE DES PETITS RUMINANTS (PPR)

•Caused by a **Morbillivirus**, related to distemper and rinderpest.
•Occurs mainly in **goats and sheep** in Africa, India, and the Middle East.
•**Lesions:**
•Similar to rinderpest in digestive tract.
•In lungs: interstitial pneumonia → may progress to catarrhal, abscess, or fibrinous pneumonia.
•**Inclusion bodies** (intranuclear + intracytoplasmic) in bronchial and alveolar epithelial cells.
•**Multinucleated giant syncytial cells** in lungs → diagnostic.

ADENOVİRUS INFECTİON

- **Dogs:**
- Type I → Infectious Canine Hepatitis.
- Type II → Respiratory disease with **necrotic bronchitis** and **intranuclear inclusion bodies (Cowdry type A)**.
- May lead to **interstitial pneumonia** and **serofibrinous exudate** in alveoli.

- **Horses:**
- Especially in **Arabian foals** with congenital immunodeficiency.
- Causes **mucopurulent exudate**, **atelectasis**, and **interstitial pneumonia**.

Microscopy: necrotic-proliferative bronchitis and intranuclear inclusions in bronchial and alveolar epithelial cells.

- Inclusions also occur in renal pelvis, ureter, conjunctiva, pancreas, and salivary glands.

HERPESVİRUS INFECTİONS

•Affect both **respiratory** and **reproductive systems**.
•Examples:
•**IBR** (Infectious Bovine Rhinotracheitis) in cattle
•**Inclusion body rhinitis** in pigs
•**Feline viral rhinotracheitis** in cats
•**Equine rhinopneumonitis** in horses

EQUİNE RHİNOPNEUMONİTİS (EQUİNE HERPESVİRUS INFECTİON)

•Also called **Mare Viral Abortion**.

•Causes **abortion (7–10 months)**, **respiratory signs**, and **neurological signs** (ataxia in foals).

Transmission: aerogenic → passes through placenta to fetus.

•**Adults:** mild upper respiratory infection.

Fetus:

•Icterus, petechial hemorrhages, subcutaneous edema.

•Focal necrosis in liver and spleen.

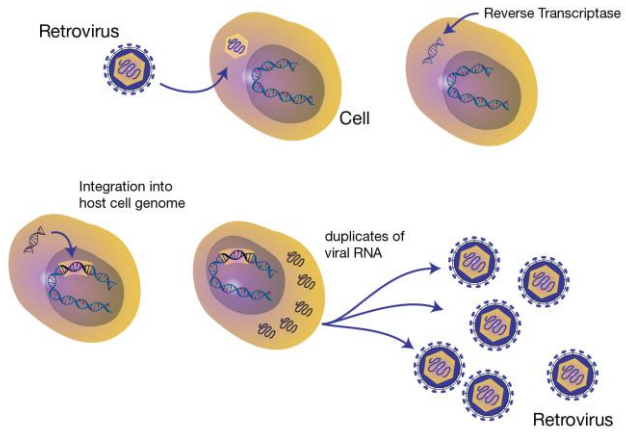
•**Intranuclear inclusion bodies** in lung, liver, spleen cells (diagnostic).

•**Foals:** may show **encephalomyelitis** and **necrotic vasculitis**.

REOVİRUS AND PARVOVİRUS INFECTİONS

•**Reovirus:** causes mild or subclinical upper respiratory infection in many species (horse, cattle, dog, cat).
•May assist in **enzootic pneumonia** as a predisposing factor.

•**Parvovirus:** in dogs and cats causes myocarditis and sometimes mild **interstitial pneumonia**.
•Other species are not significantly affected in the respiratory system.



RETROVIRUS INFECTIONS

- These infections cause **chronic interstitial pneumonia**, **arthritis**, and **mastitis**.
- Other findings such as **encephalitis** can also occur.
- Some retroviral diseases show **inflammatory-neoplastic changes**.

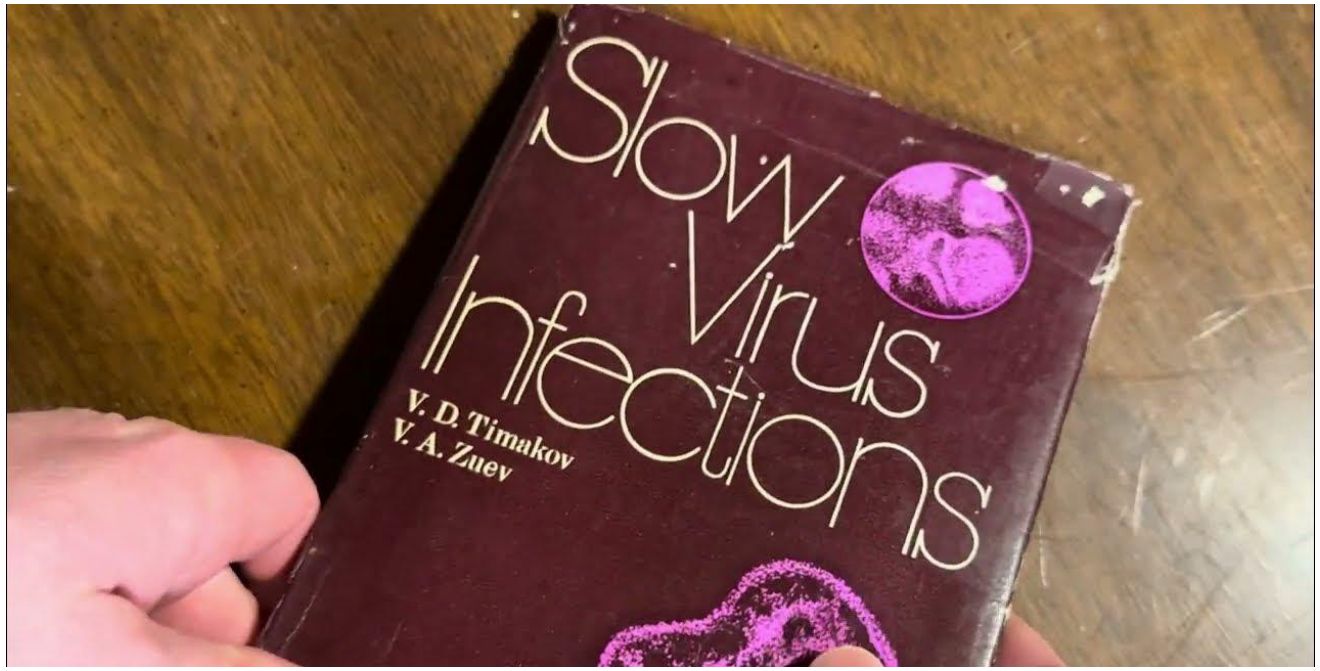
Main Diseases

- **Ovine Progressive Pneumonia (Maedi-Visna)**
- **Caprine Arthritis-Encephalitis (CAE)**
- **Pulmonary Adenomatosis of Sheep**

OVINE PROGRESSIVE PNEUMONIA (MAEDI-VISNA)

Causative Agent:

- *Lentivirus*, a type C **fragmented retrovirus**.
- It develops **slowly** and causes **long-term infection** (called a *slow virus infection* due to prolonged incubation).



Case Records
of the
Massachusetts General Hospital

EDITED BY RICHARD C. CABOT, M.D., AND HUGH CABOT, M.D.

F. M. PAINTER, ASSISTANT EDITOR

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICO-PATHOLOGICAL EXERCISES

CASE 9431

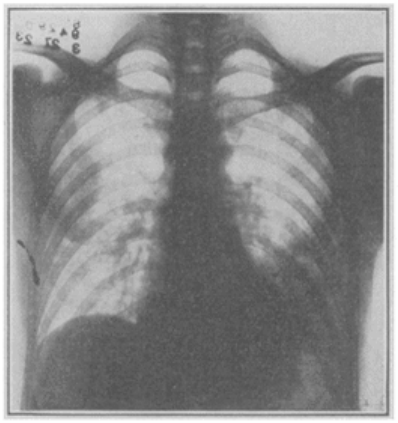
An American student of twenty-four entered March 26, 1923, complaining of pain and dyspnea.

F. H. and P. H. Not recorded.

P. I. On the afternoon of March 23 the patient had a severe cold with moderate headache and backache. He felt quite weak. He stayed in bed until noon next day and remained in his room all day. March 25 he stayed in bed all day and took aspirin, ten grains every four hours. This gave considerable relief to the headache and backache. That afternoon he noted dry unproductive cough for the first time. He felt very weak and thought he had fever. About four o'clock he had a chill that made him shake considerably and hunched him up in a knot. At three o'clock on the day of admission he awoke with severe pain just below the ensiform associated with and aggravated by unproductive cough. Breathing was difficult, and deep breathing aggravated the pain. A physician applied adhesive plaster to his chest with great relief to the pain.

P. E. (Because of his condition the examination was incomplete and unsatisfactory.) A fairly well developed and nourished, acutely ill, highly nervous young man wrapped up in several blankets, shivering. Breathing rapid, shallow, labored, painful. Skin dry and hot. Very slight pyorrhea. Throat somewhat injected. Tonsils absent. Frequent paroxysms of racking cough which caused excruciating pain chiefly under the lower sternum, with production of small amounts of pinkish, thick, slightly purulent sputum. Apex impulse of the *heart* seen and felt in the fifth space 8 cm. to the left of the midsternum in the midclavicular line. No enlargement to percussion. Sounds rapid, regular, of good quality. Soft systolic murmur at the apex, not transmitted. *Lungs.* Expansion greater on the left. Diminished breathing at the right back from the lower third of the scapula down. No definite dullness or change in character of breath sounds made out. No râles or friction rub heard. *Abdomen* negative except for scar of hernia operation on the left side. *Genitals, extremities, pupils* and *reflexes* normal.

T. 103.1°-105.5°, rectal. *P.* Steadily rising, 92-145. *R.* 28-58. *Urine.* ℥ 24 on the one occasion recorded. Sp. gr. 1.032. No albumin or sugar, two or three leucocytes per high power field and a few hyalin casts. *Blood.* Hgb. 90%. Leucocytes 14,500-3,700. Polynuclears 79%.



9431

Area of dullness at left base occupying the costophrenic angle and obscuring the heart apex and diaphragm. The outline of the diaphragm below is suggested by the gastric gas bubble seen beneath it. Upper limit of area of dullness is indefinite and has not the characteristic position and outline of fluid. In the lung above it and diminishing upward are small areas of mottled dullness extending to the lung root, which is increased in size and density. On the right side scattered throughout the lower two-thirds of the lung field, most marked in the lower half, are numerous shadows of mottled dullness.

Two *blood cultures* negative. *X-ray.* (See illustration.) "The findings are probably due to a pathological process in the lung parenchyma, most marked in the left base. . . . Shadows in the remainder of the lung fields are suggestive of a scattered infectious condition throughout both lungs probably of the same nature as the denser area noted. There is no evidence of free fluid, but there may be a small amount of fluid in the left base."

The day after admission Dr. W. H. Smith noted, "Very ill. Dyspnea with pain on inspiration. No focus found for aureus infection. No costovertebral tenderness. No palpable kidney. Abdominal muscles held rigid, probably from pleural pain. Two small hyperemic papules, one on the left palm, the other on the right index finger. The systolic apical bruit appears harmless. . . . At the right base some dullness, suggesting fluid rather than consolidation. Serious outlook." That afternoon the house officer could make out no abnormal signs in the lungs. The patient was raising considerable amounts of sputum colored uniformly with

OVINE PROGRESSIVE PNEUMONIA (MAEDI-VISNA)

History:

- **Maedi** ("dyspnea" – USA, 1923): progressive interstitial pneumonia.
- **Visna** ("wasting" – Iceland, 1957): necrotic non-purulent encephalitis.

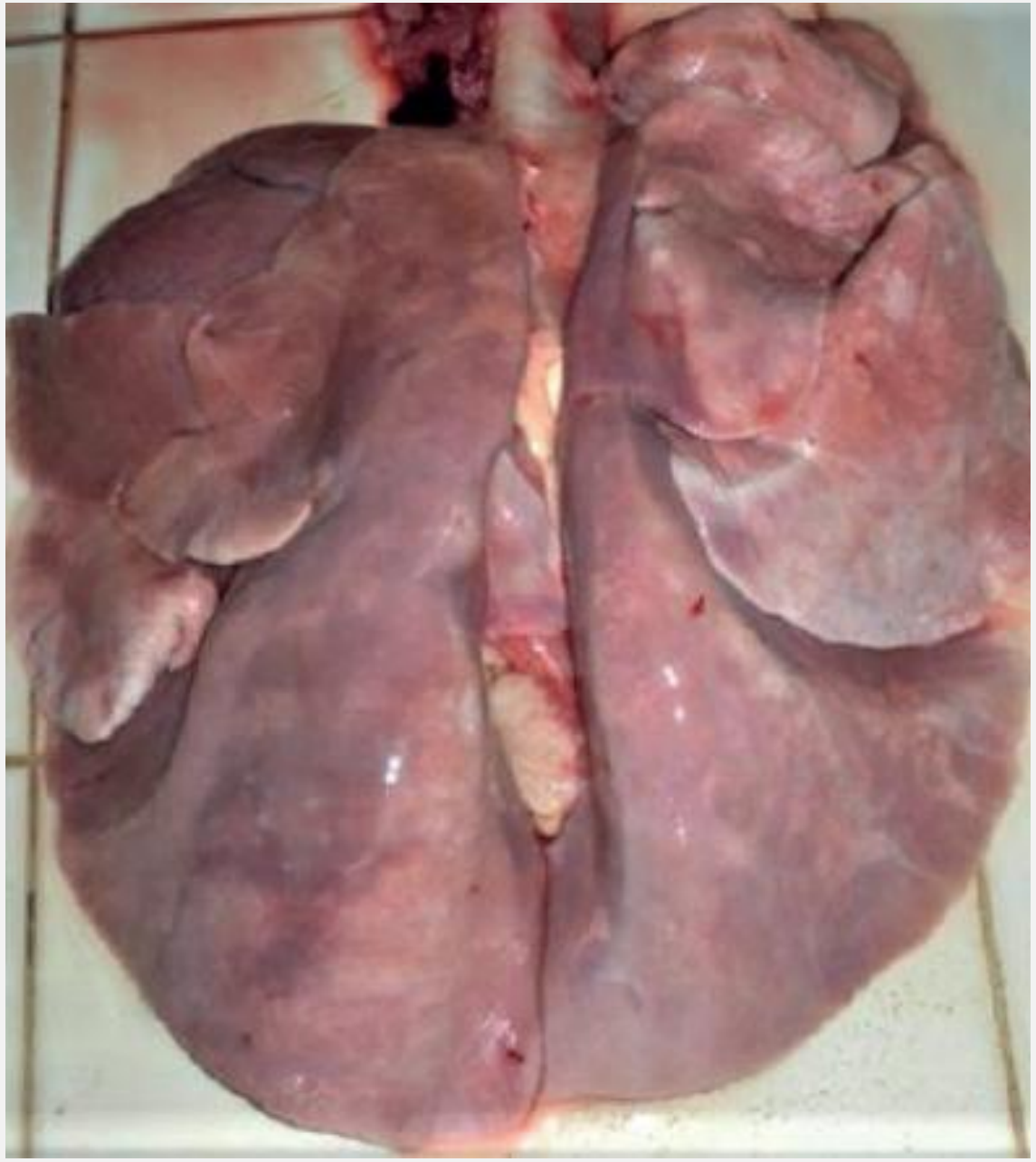
Later discovered as two forms of the same lentiviral disease.

Associated Conditions (similar to CAE in goats):

- **Chronic proliferative arthritis**
- **Chronic mastitis** with lymphoid cell infiltration resembling lymph nodes in mammary tissue.

Clinical Findings:

- **Endemic** disease that progresses **slowly**.
- Does **not occur in animals under 2 years old** (long incubation period).
- **Dry cough**, **dyspnea**, and **weakness** are the major signs.



Borquez Cuevas, M. Y., Hernández Chávez, J. F., Armenta Leyva, B., Cedillo Cobián, J. R., & Molina Barrios, R. M. (2021). Ovine Progressive Pneumonia: Diagnosis and Seroprevalence in the South of Sonora, Mexico. *Case reports in veterinary medicine*, *2021*(1), 6623888.

PATHOLOGICAL FINDINGS

Macroscopic Findings:

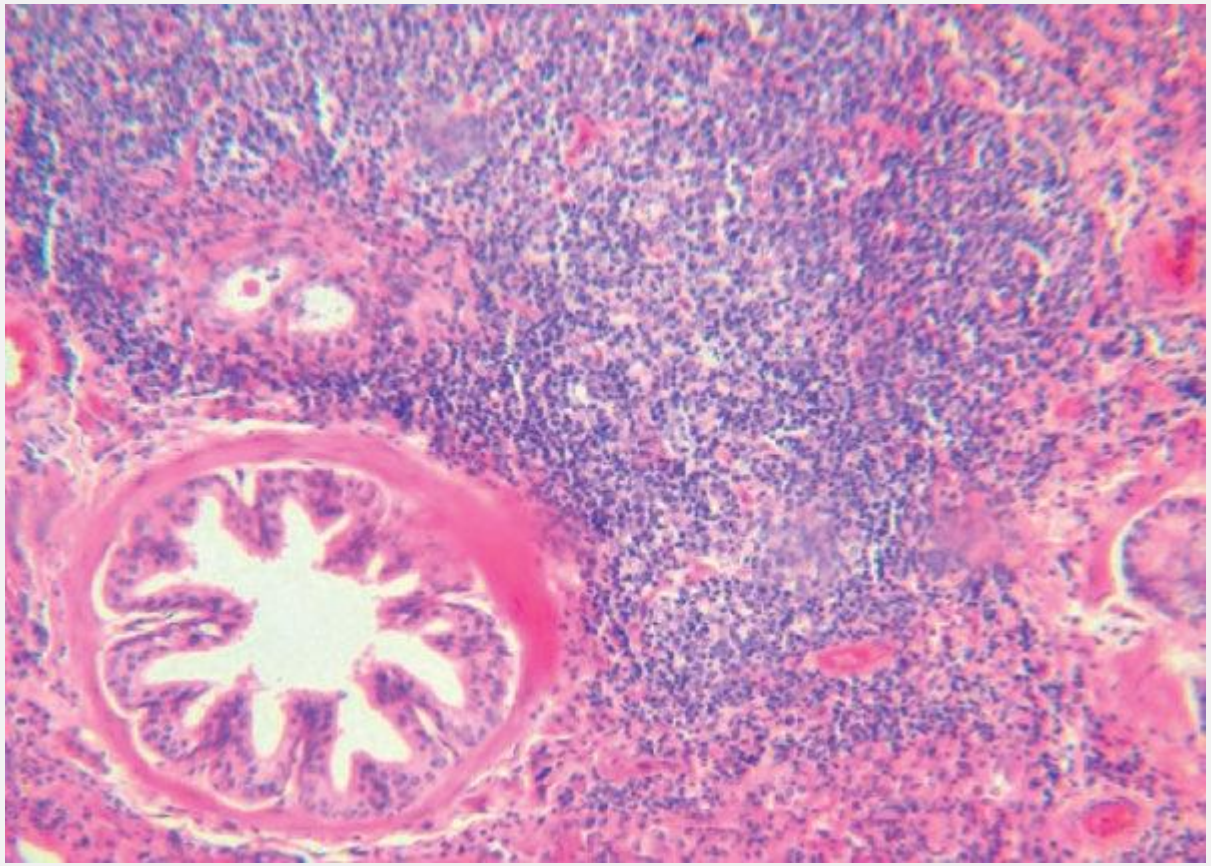
- Lungs are **pale pink**, **heavy**, and have **poor collapse**.
- **Rubbery consistency**.
- Lesions mainly in **dorsal lung areas**.
- On section, there are **pin-sized gray-white or gray-red nodules** scattered and circumscribed.
- **Bronchi contain mucus**.
- **Regional lymph nodes enlarged.**

Gross appearance of ovine progressive pneumonia in the lung of a sheep. **The affected lung is enlarged and heavy and has no collapse, with rib impressions on the costal surfaces** of the diaphragmatic lobes.

HİSTOPATHOLOGİCAL FİNDİNGS

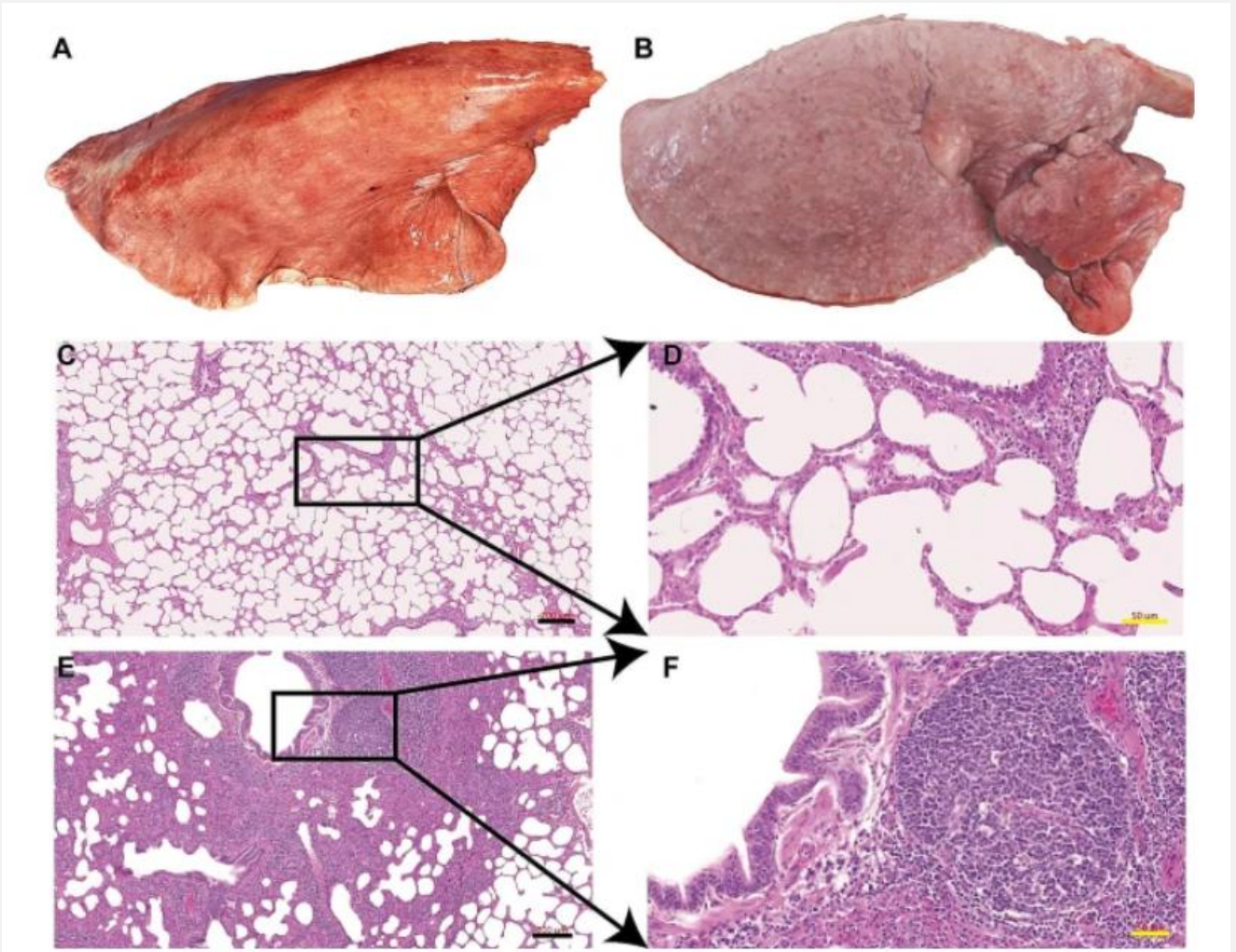
Histopathological Findings:

- **Peribronchial** and **perivascular** **connective tissue proliferation** in the interstitium.
- Infiltration of **lymphocytes** and **mononuclear cells** forming **lymphoid follicle-like foci**.
- **Peribronchial lymphoid hyperplasia** and **smooth muscle hypertrophy** in bronchi.
- **Fibrosis** in interlobular regions.
- **Hyperplasia** of **alveolar type II cells** and **bronchiolar epithelial cells**, especially in alveolar ducts.
- **Lymph nodes:** chronic lymphadenitis and follicular hyperplasia.



Ovine progressive pneumonia: **peribronchiolar lymphoid hyperplasia** with formation of prominent well-defined lymphoid nodules and **smooth muscle hyperplasia** of the bronchiolar wall (H&E, 100x).

Borquez Cuevas, M. Y., Hernández Chávez, J. F., Armenta Leyva, B., Cedillo Cobián, J. R., & Molina Barrios, R. M. (2021). Ovine Progressive Pneumonia: Diagnosis and Seroprevalence in the South of Sonora, Mexico. *Case reports in veterinary medicine*, *2021*(1), 6623888.



Histopathologic characteristics of Maedi-visna virus (MVV)-infected lungs. (**A**) Overall appearance of the lung from a healthy sheep; (**B**) appearance of Maedi-visna disease in an infected sheep lung sample; (**C** and **D**) microscopic examination of the lung from a healthy sheep (black bar, 200 μm; yellow bar, 50 μm); (**E** and **F**) microscopic view of MVV-infected lungs (black bar, 200 μm; yellow bar, 50 μm)

Shi, X., Zhang, Y., Chen, S., Du, X., Zhang, P., Duan, X., ... & Liu, S. (2024). Differential gene expression and immune cell infiltration in maedi-visna virus-infected lung tissues. *BMC genomics*, *25*(1), 534.

JAAGSİEKTE (OVİNE PULMONARY ADENOMATOSİS)

- Jaagsiekte, also known as **Ovine Pulmonary Adenomatosis (OPA)**, is an **infectious neoplastic disease** of sheep characterized by the development of **bronchioalveolar adenomas or adenocarcinomas**.
  The tumors may metastasize to **regional lymph nodes**, and in some cases, to **extrathoracic lymph nodes** and **other organs**.
  The neoplastic cells originate mainly from **type II pneumocytes** and partly from **bronchial Clara cells**, therefore they are **cuboidal to columnar in shape** and show **papillary proliferation**.

ETIOLOGY

- The causative agent is a **retrovirus of the Lentivirus group**, previously referred to as **Jaagsiekte sheep retrovirus (JSRV)**.
  (Older texts mention bovine herpesvirus type 4, type B or D, but the true agent is a retrovirus).

CLİNİCAL FİNDİNGS

•The disease has a **chronic course**.
•It is usually observed in sheep aged **7 months to 10 years**, most commonly around **3 years**.
•Clinical signs resemble those of **ovine progressive pneumonia (Maedi-Visna)**, including:
•**Progressive dyspnea**,
•**Coughing**,
•**Weight loss and weakness**,
•**Increased respiratory effort**, especially after exercise.
•The disease is **progressive and fatal**.

PATHOLOGICAL FINDINGS

Macroscopic Lesions

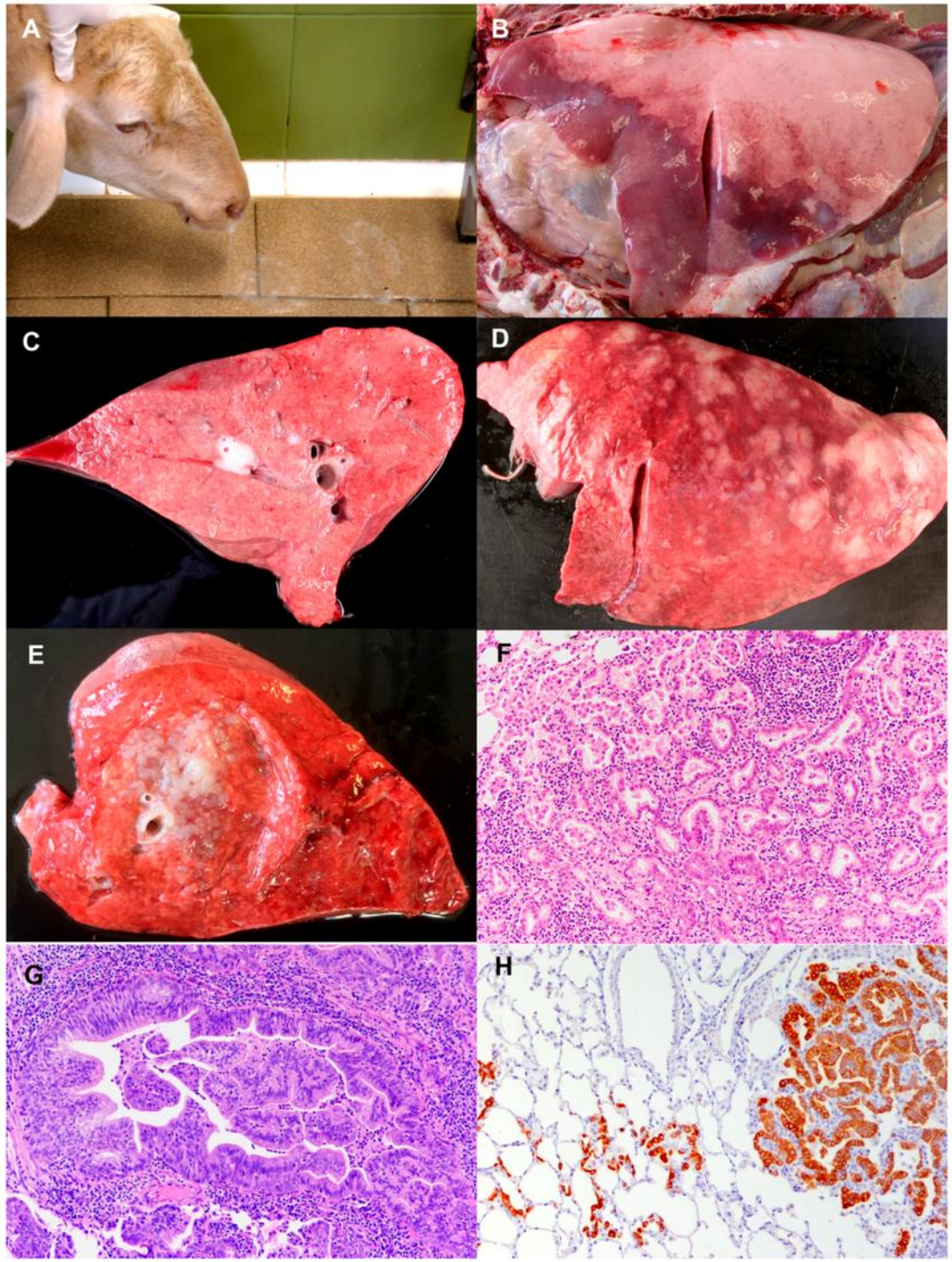
- The **diaphragmatic lobes** are the **primary predilection site**.
- Lesions spread ventrally to the **left cardiac** and **right accessory lobes** over time.
- **Early stage:**
- In the affected areas, **soft, grayish-transparent, non-calcified nodules** appear, about the size of lentils.
- The intervening lung tissue remains normal.
- **Advanced stage:**
- The number of nodules increases, and they coalesce to involve the **entire lobe**.
- The affected regions are **dull, porcelain-white**, and have a **rubbery consistency**.
- The normal lung, which normally weighs **300–800 g**, may reach up to **3 kg** in affected cases.
- When pressed, the **cut surface exudes serous fluid**.
- In about **4% of cases**, metastases occur in the **regional lymph nodes**.

MİCROSCOPİC LESİONS

- There are two types of histological changes: **neoplastic** and **non-neoplastic**.

Neoplastic Areas

- The tumor exhibits a **bronchioalveolar adenoma or adenocarcinoma** pattern.
- **Alveolar walls** are lined by **cuboidal or columnar epithelial cells**.
- **Papillary proliferations** develop within some bronchi and alveoli.
- In metastatic cases, lesions may show **cystic papillary adenoma**-like structures.
- The **stroma** consists of **delicate connective tissue**, sometimes showing a **myxomatous appearance**.
- **Lymphocytes and histiocytes** may be present around neoplastic foci.



Ovine pulmonary adenocarcinoma (OPA): clinical signs and pathology. (A) Four year old sheep showing OPA clinical signs. When head is lowered, frothy sero-mucous fluid comes from the nostrils and pours over the floor. (B) **Post-mortem examination of thoracic cavity**. Classical OPA form. Left lung with cranio-ventral areas purple in colour and consolidated. The rest of the lung shows an increase in volume and is lighter in colour. (C) **Right caudal lung section**. Classical OPA. Lung section showing granular appearance foci and foamy fluid pouring from main airways. (D) **Left lung from a sheep showing atypical OPA form.** Multiple white nodules of various sizes distributed throughout the lung surface. (E) Section of lung from **right caudal lobe. Atypical OPA**. Multiple white nodules with various sizes: bigger ones coalescing close to a central main bronchus and others expanding to close lung areas.

(F) Histopathology of OPA lesion. **Alveolar epithelial cells proliferate following a lepidic pattern. Alveolar wall is replaced by cuboidal cells into a tubular or papiliform pattern. Tumour stroma is infiltrated mainly by lymphocytes. Numerous macrophages are filling alveolar lumens in the tumours and in the close areas.** Hematoxylin-eosin. 100×. (G) Histopathology of OPA lesion. **Bronchiole with epithelium transformed into papiliform growth almost completely filling the lumen**. Hematoxylin-Eosin. 100×.

(H) Immunohistochemistry using a mouse monoclonal **antijaagsiekte sheep retrovirus envelope (JSRV Env) protein. Cellular membranes and cytoplasms of neoplastic cells of a tumour nodule are labelled.** In the adjacent alveoli, positive cells are observed either isolated or in small groups. 100×.

De las Heras, M., Borobia, M., & Ortín, A. (2021). Neoplasia-associated wasting diseases with economic relevance in the sheep industry. *Animals*, *11*(2), 381.

Non-Neoplastic Areas

- Represent changes associated with **desquamative and progressive interstitial pneumonia**.
- **Alveolar septa** are thickened due to infiltration by **mononuclear inflammatory cells**, mainly lymphocytes and macrophages.
- Occasional **granulocytes** may also be found.
- Some alveoli contain **edematous fluid**, and **secondary bacterial infections** may occur.

DİFFERENTİAL DİAGNOSİS

- **Verminous pneumonia (lungworm infection)** — because of nodular, grayish lung lesions.
- **Maedi (Ovine progressive pneumonia)** — due to similar chronic interstitial and fibrotic lung changes.

However, **Jaagsiekte** can be distinguished by:

- The presence of **neoplastic epithelial proliferation** (adenomatous or papillary),
- **Absence of significant fibrosis**,
- **Presence of tumor metastasis**, and
- Identification of **JSRV antigen** by immunohistochemical or molecular methods.

EQUINE VIRAL ARTERITIS

•Caused by **Arteritis Virus** from the **Togaviridae** family.
•Sometimes called **“Pinkeye”** or **“Thymus disease of horses.”**
•Produces **generalized lesions** with **fibrinoid degeneration of small arteries** and **inflammatory infiltration**.
•**Lung edema** and, in about **10% of cases**, **interstitial pneumonia** develop.
•**Secondary bacterial infections** (*e.g., Streptococcus*) may lead to **necrotic or catarrhal pneumonia.**

AUJESZKY'S DISEASE (PSEUDORABIES)

- Caused by **Porcine Herpesvirus Type I (Herpesviridae family)**.
- Main lesions occur in the **nervous system**, but **interstitial pneumonia** may also develop.
- In this pneumonia, inflammation is **intra-alveolar**, not peribronchiolar or perivascular.
- **Histopathology:**
  - **Mononuclear and eosinophilic granulocyte infiltration** in alveolar septa.
  - **Necrosis** in interstitial areas may be seen.

OTHER VIRAL INFECTIONS

- Some **enteric viruses** may also cause pneumonia:
  - **Enteroviruses**
  - **Coronaviruses**
  - **Parvoviruses** (in cats and dogs)
  - **BVD/MD viruses (Bovine Viral Diarrhea / Mucosal Disease)**
- **BVD virus** is **immunosuppressive**, predisposing animals to **secondary respiratory infections**.

INFECTIOUS BOVINE RHINOTRACHEITIS (IBR)

Also Known As:

- *Infectious Pustular Vulvovaginitis (IPV)*
- *Necrotic Rhinitis*
- *Red Nose Disease*

Etiology:

- Caused by **Bovine Herpesvirus-1**.

Lesions and Clinical Forms:

- **Rhinotracheitis:** inflammation and necrosis of nasal and tracheal mucosa.
- **Bronchopneumonia**
- **Conjunctivitis**
- **Vulvovaginitis** and **balanoposthitis** (inflammation of genital mucosa).
- **Abortion** may occur due to fetal infection.

Pathological Findings:

- **Fibrinonecrotic rhinitis, laryngitis, tracheitis.**
- **Intranuclear inclusion bodies** found in respiratory epithelium.
- **Necrotic lesions** in epiglottis, buccal mucosa, gums, vagina, penis, and prepuce.
- **Diffuse hemorrhages** in aborted fetuses.

Gross Appearance:

- *Red nose*, *nasal discharge*, *ulcers* in oral and genital mucosa.
- In severe cases, necrosis and pustules appear in respiratory and genital tracts.
- **Aborted fetuses** may show **hemorrhages** and **necrosis** in several organs.

CALICIVIRUS INFECTION (CATS)

- Caused by **Feline Calicivirus**.
- Leads to **multifocal ulcerative glossitis** and **broncho-interstitial pneumonia**.
- Often coexists with feline herpesvirus infections as part of the **Feline Respiratory Disease Complex**.

BOVINE'S OTHER INTERSTITIAL PNEUMONIAS

- In addition to **viral** and **parasitic pneumonias**, there are two other important forms of **interstitial pneumonia** in cattle that differ in their **etiology**.
  These are categorized according to their **duration** as **acute** and **chronic interstitial pneumonias**.
- Morphologically, interstitial pneumonia includes **edema** and **exudative changes** in addition to typical inflammatory lesions.
  Therefore, these forms are referred to as **acute atypical interstitial pneumonia** and **chronic atypical interstitial pneumonia**.
- According to the **cause (etiology)**, these diseases are also grouped under **allergic** and **toxic pneumonias**.

ACUTE ATYPİCAL INTERSTİTİAL PNEUMONİA

- This disease is also known as **Fog Fever**.
  It occurs in **cattle grazing on lush pastures** (after being kept indoors) and is associated with **pulmonary edema and emphysema**.
  The word **"Foggage"** means **stubble or dry grass remaining after harvest**, hence the alternative name *Stubble Harvest Fever*.

- **Etiology**
- The disease develops due to the **toxic effects of L-tryptophan**, which is converted in the rumen to **3-methylindole**.
  Although primarily toxic in nature, it may also involve an **allergic component**.
  The inhaled or absorbed toxins cause **severe injury** to the lung tissue.

- **Pathogenesis and Morphology**
- The condition is characterized by **damage to pneumocyte type II cells**,
- Formation of **hyaline membranes**,
- **Atelectasis** (collapse of alveoli), and
- **Diffuse pulmonary emphysema**.
- Because of these changes, this condition is defined as **acute atypical interstitial pneumonia**.

CHRONİC ATYPİCAL INTERSTİTİAL PNEUMONİA

- This condition develops as a result of **allergic reactions** to **microbial or fungal antigens** present in barn environments.
  It is caused by species such as:
- *Actinomyces spp.* (especially *Micropolyspora faeni* and *Thermoactinomyces vulgaris*)
- *Aspergillus spp.* (especially *Aspergillus fumigatus* and *Aspergillus niger*)
- Because of its **allergic** basis, it is referred to as **"Allergic Pneumonia"**.
- It is also known by other names:

Bovine Allergic Alveolitis

Bovine Hypersensitivity Pneumonia

Farmer's Lung

FARMER'S LUNG (BOVİNE ALLERGİC ALVEOLİTİS)

- Occurs in **winter**, when cattle are housed indoors and fed with **moldy or dusty hay**.
- The disease results from **inhalation** of microorganisms such as *Micropolyspora faeni*, *Thermoactinomyces vulgaris*, and *Aspergillus* species found in cowhouse bedding and feed.
- The immune response involved is a **Type III (immune complex) hypersensitivity reaction**.

Macroscopic Findings

- The **lung volume is increased**.
- Lesions may involve **entire lobes** or large areas of the lung.
- Affected regions appear **yellowish**, **edematous**, or **elastic** in consistency.
- **Surrounding areas are emphysematous.**
- **Bronchial lumens** contain **yellowish mucus**.

Microscopic Findings

- Infiltration of **lymphocytes**, **plasma cells**, and **eosinophilic granulocytes**.
- **Bronchiolar obliteration** may occur due to inflammation.
- In the **interstitial tissue**, there are numerous **mononuclear cells** (macrophages, lymphocytes, plasma cells) and **eosinophilic granulocytes**.
- Occasionally, **multinucleated giant cells** are present.
- In chronic cases, **fibrocytes** and **fibroblasts** appear, indicating **fibrosis**.

Morphologically, the lesion resembles ordinary interstitial pneumonia but differs by its **exudative** and **allergic** nature, hence the term **chronic atypical interstitial pneumonia**. Over time, **fibrous tissue proliferation** marks the chronic stage.

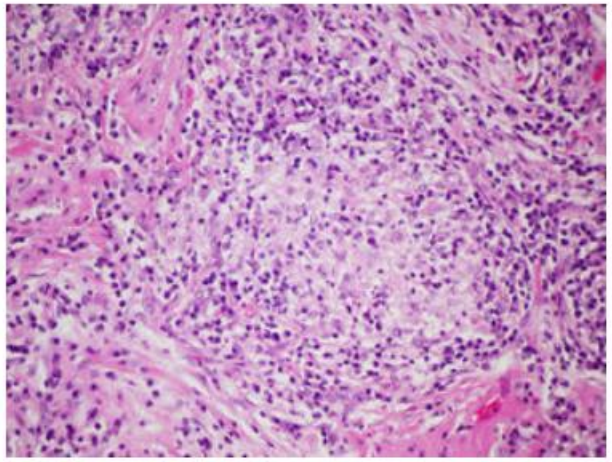


Fig. 4.

Histopathological characteristics in farmer's lung disease. Loose, non-necrotizing granulomas formed by histiocytic aggregates and abundant lymphoplasmacytic infiltrate (hematoxylin-eosin 40×).

Cano-Jiménez, E., Acuña, A., Botana, M. I., Hermida, T., González, M. G., Leiro, V., ... & Sanjuán, P. (2016). Farmer's lung disease. A review. *Archivos de Bronconeumología (English Edition)*, *52*(6), 321-328.

EQUİNE ALLERGİC PNEUMONİA

- This condition in horses is **similar to Farmer's Lung** in cattle.
  It is also caused by **inhalation of antigens** such as dust, molds, or fungal spores, leading to an **allergic hypersensitivity reaction** in the lungs.

ALLERGİC PNEUMONİA (GENERAL CONCEPT)

- **Allergic pneumonia** occurs due to **antigenic substances** of **plant or animal origin**.

These allergens include:

- Dust, pollen, and mold spores
- Insects and helminths
- Bacteria, fungi, and viruses

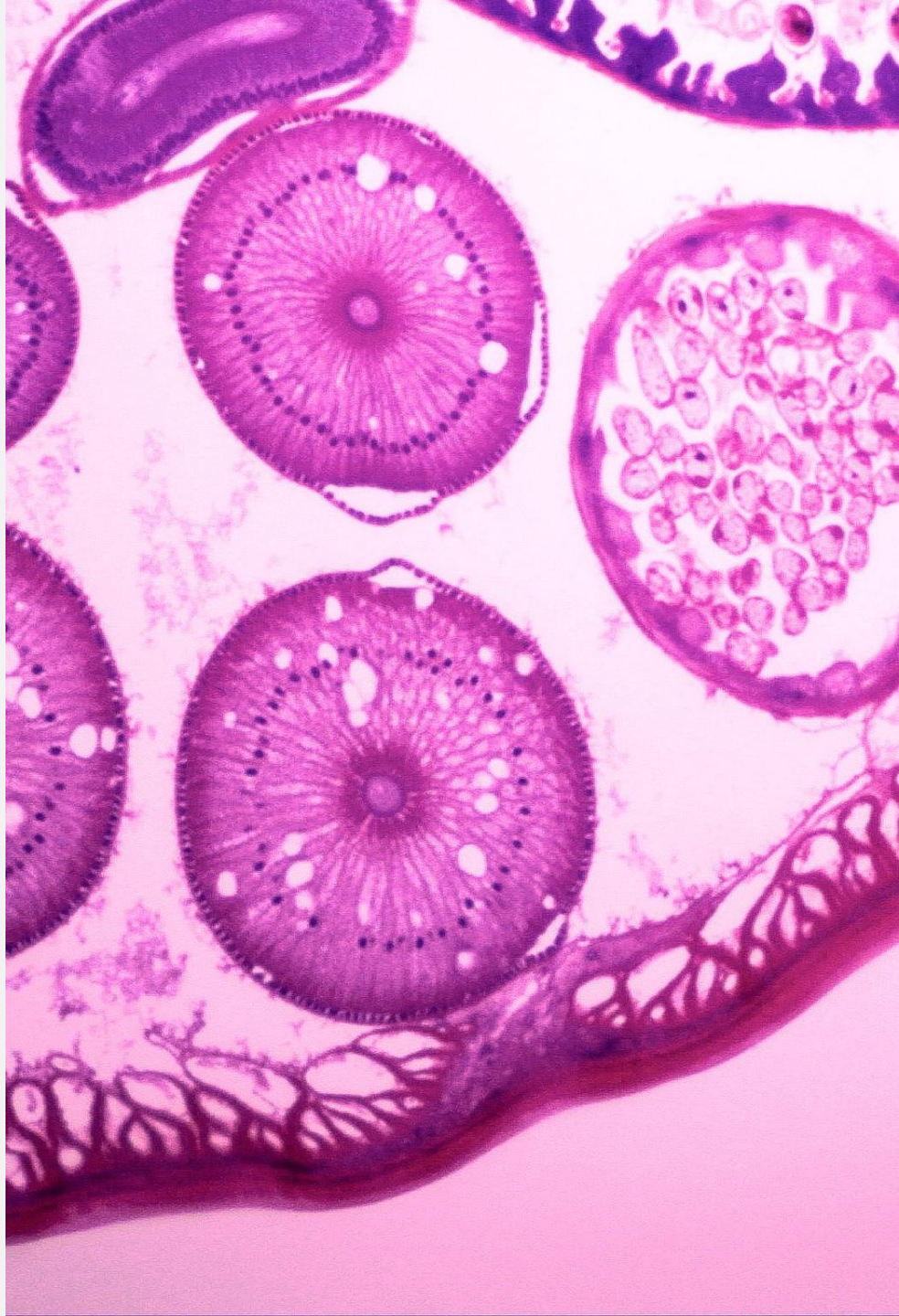
Examples of diseases caused by this mechanism include:

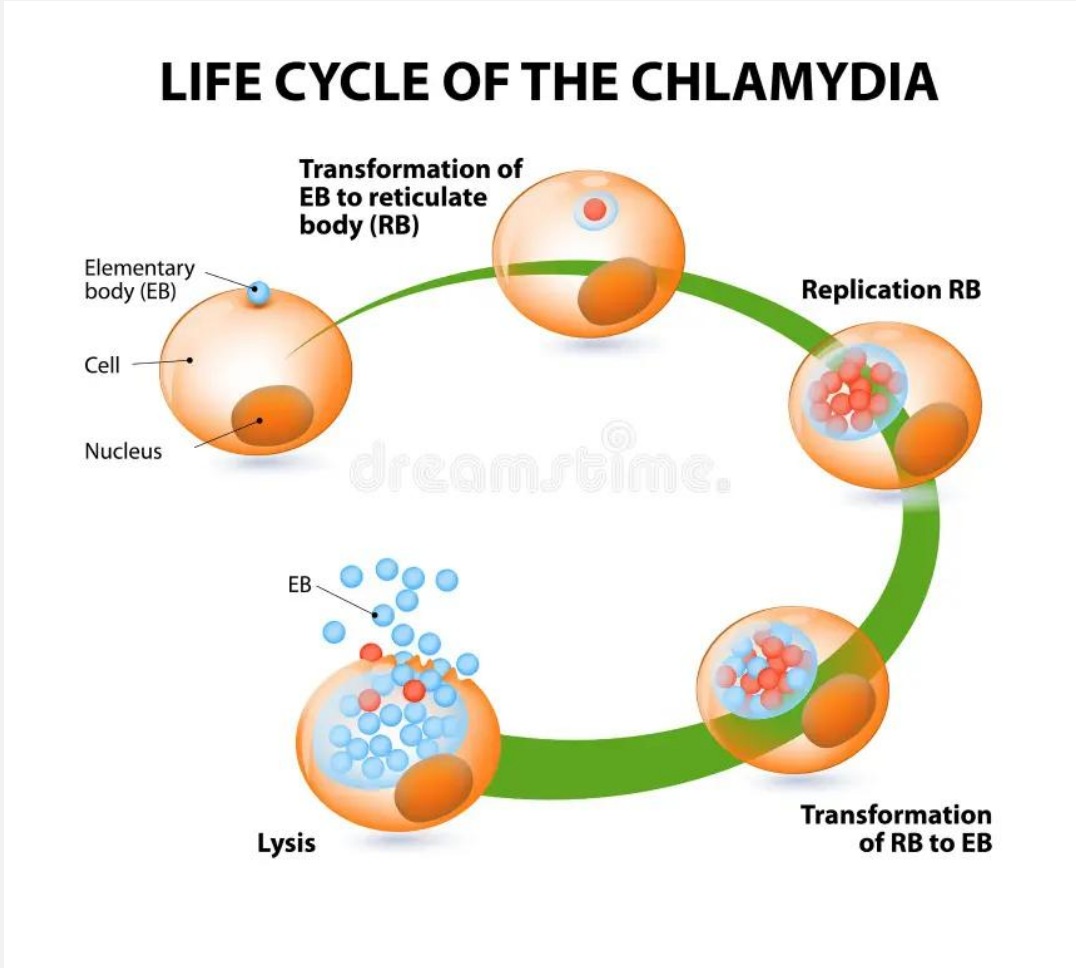
- **Farmer's Lung** in cattle
- **Equine Pulmonary Emphysema**
- **Equine Allergic Pneumonitis**
- **Asthma bronchiale** in humans
- **Dictyocaulus viviparus** infection in cattle (as a hypersensitivity response)
- These pneumonias are **etiologically allergic** but **morphologically interstitial**, often showing:
- **Eosinophilic granulocyte infiltration**, and
- **Various types of pulmonary emphysema**.

CHLAMYDIOSIS

General Information

- **Chlamydia psittaci** has a **wide host spectrum**, affecting both **avian** and **mammalian species**, including **humans**.
  Unlike ordinary bacteria, it **multiplies in tissue cultures** and **embryonated chicken eggs**.
  It contains **both DNA and RNA**, and although it stains like **Gram-negative bacteria**, it differs in structure and reproduction.
- During multiplication, the organism forms **distinct bodies** within the host cell.





- *Chlamydia pneumoniae* is a small gram-negative bacterium with two main forms in its life cycle.
- The **elementary body (EB)** is the inactive but infectious form that survives outside the host and spreads through droplets to the lungs. Inside host cells, the EB enters an **endosome** and transforms into a **reticulate body (RB)**, which uses host cell metabolism to multiply.
- The RBs then revert to EBs, which are released when the host cell dies, allowing infection of new cells or new hosts. Thus, **EBs infect**, while **RBs replicate**.

•**Life cycle**:

- **Elementary body (EB):** infectious, metabolically inactive, spore-like
- **Reticulate body (RB):** non-infectious, metabolically active, replicative form (seen only within host cells)

PATHOGENESİS AND HİSTOPATHOLOGY

- **Chlamydial organisms** are often found in **trophoblastic cells** of the **sheep fetus**.

Clinical findings are **nonspecific**.

- In domestic animals, infection generally causes **chronic broncho-interstitial pneumonia**. However, secondary bacterial infections may lead to **catarrhal-purulent bronchopneumonia**.

Histologically:

- The **interstitial areas** show **lymphoplasmacytic infiltration**, forming **focal lymphoid follicle-like structures**.
- **Type II pneumocytes** are **hyperplastic**.
- In **bronchi and alveoli**, exudate containing **neutrophilic leukocytes** is common.
- The agent can be demonstrated using **special stains** or **immunohistochemical methods** (e.g., immunofluorescence).

INFECTİON İN DOMESTİC ANİMALS

Cattle, sheep, and goats:

- Isolated from cases of **enzootic pneumonia**.
- May also cause **enteritis**.

In calves:

- Similar pulmonary lesions occur, accompanied by:
  - **Polyarthritis** (joints of limbs, vertebrae, and mandible),
  - **Meningoencephalomyelitis**, and
  - **Perisplenitis**.

In cows:

- Causes **abortion**, resulting from **placental infection**, usually at **7–8 months of gestation**.

Fetal findings:

- **Subcutaneous edema**,
- **Increased pleural and peritoneal fluid**,
- **Swollen lymph nodes**,
- **Splenomegaly**,
- **Petechiae** on oral mucosa, conjunctiva, larynx, and trachea,
- **Loose nodules in the liver**.

In sheep:

- Similar to cattle.
- Causes **follicular conjunctivitis**.

In foals (horses):

- Causes **polyarthritis**.

In dogs:

- Leads to **polyarthritis**, **hepatic necrosis**, **lymph node and splenic reticuloendothelial (RES) hyperplasia**, and **leptomeningitis**.

In cats:

- Produces **chronic conjunctivitis**, **rhinitis**, and **subclinical broncho-interstitial pneumonia**.

In rabbits:

- Causes **enzootic pneumonia**.

In Birds

- Known as **Psittacosis** or **Ornithosis**.
- Most common in **pigeons**, often **latent (subclinical)**.
- The disease becomes active under **stress**, such as during:
  - The **molting period of young birds**,
  - **Transportation**, or
  - **Poor environmental conditions**.
- Transmission occurs via **inhalation of dust containing infected feces**.

Lesions in birds:

- **Rhinitis**,
- **Firm areas in the lungs**,
- **Enlarged liver** with **yellowish-brown foci**,
- These are generally **nonspecific lesions**.

In Humans

- The disease occurs most often in people who have **close contact with birds**, such as **bird breeders**, hence the name **"Bird Fancier's Disease."**
- It also affects **poultry farm** and **slaughterhouse workers**.
- **Transmission:**
- Mainly by **inhalation of dust containing dried feces** of infected birds.
- It can also spread through **sputum of infected persons**.
- **Incubation period:** approximately **20 days**.

Clinical Course in Humans

- **Mild cases:**
- Sudden onset of **fever**, **sore throat**, **fatigue**, **photophobia**, and **severe headache** (flu-like symptoms).
- Recovery occurs within a few days.
- **Severe cases:**
- May develop **atypical interstitial pneumonia** and **typhoid-like enteritis**.
- Sometimes **fatal**, particularly in **elderly patients**, with a **mortality rate up to 20%**.