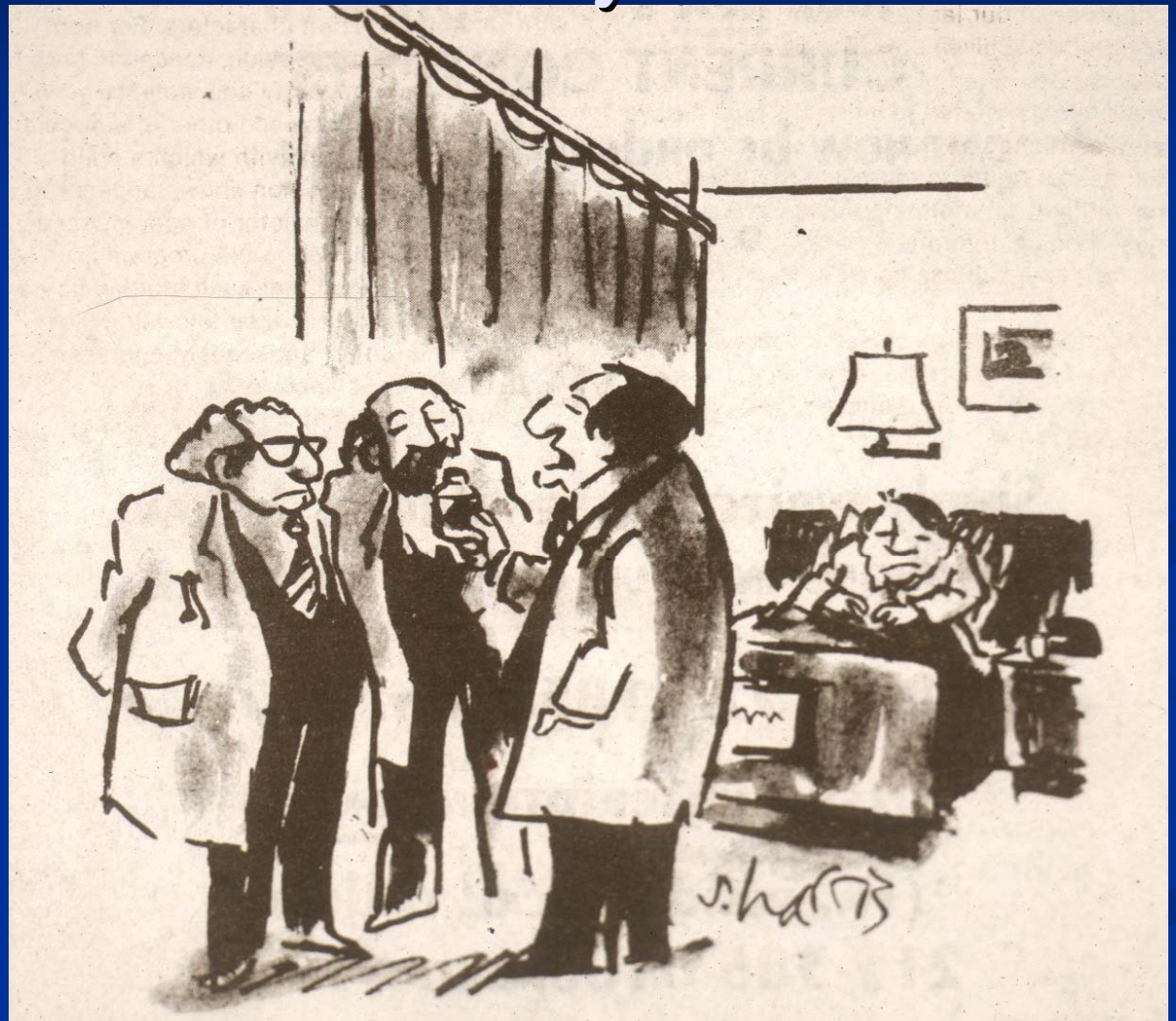
Respiratory Pathology of Laboratory Animals



"Don't forget, this medicine worked better on the rat than it did on the guinea pig, and I think he's more like a guinea pig."

Introduction

- The mouse is now the preferred species for most biomedical research, so the mouse lung has become the focus of basic research, toxicology and drug development.
- While the mouse is genetically closely related to man, it differs in lung anatomy, physiology, and immunology.

Introduction (cont.)

- Reasons for use of mice for pulmonary research
  - Technology for over expression or ablation of target genes.
  - Mouse gene defect leading to disease phenotype may translate to human genotype responsible for disease.
  - Increased understanding of mouse immune system.

Creation of GEM Pulmonary Models

- Lung directed – e.g. Clara cell 10kDa (CC10) protein promoter
- Externally regulated – e.g. tetracyline-inducible (use of two transgenic constructs) – for timing of expression. Allows adult, rather than developing lung to be targeted.
- Often used together with exogenous agent such as cigarette smoke, infection

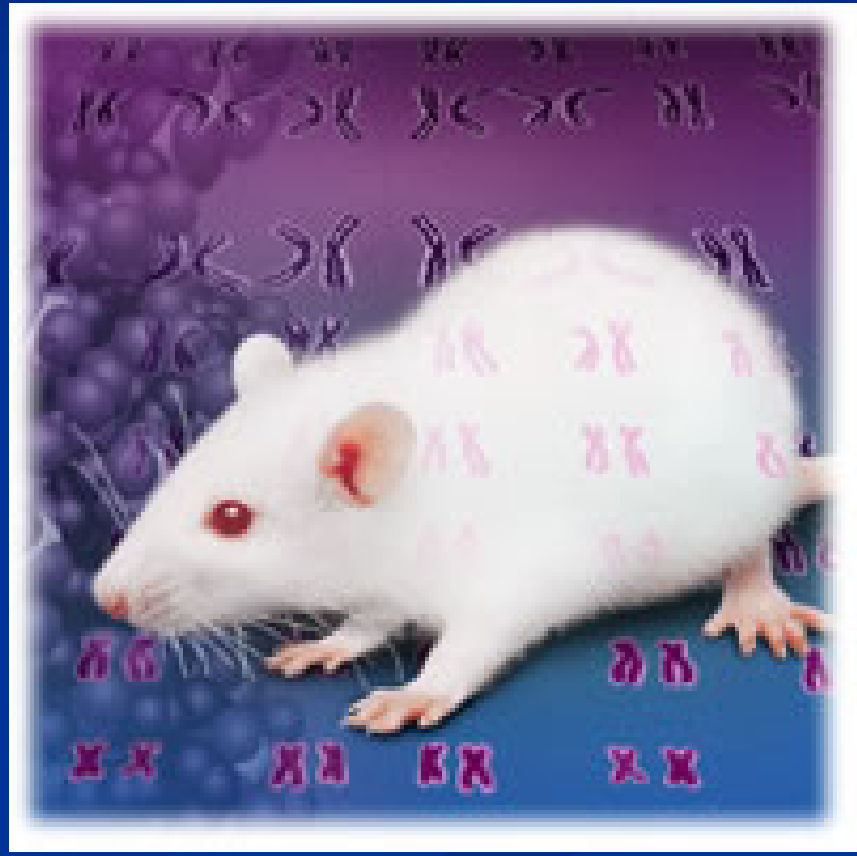
Advent of Genetically Engineered Mice (GEM)

- Increased prevalence of mouse pathogens
  - Increased trafficking of mice among laboratories
  - Increased susceptibility of GEM to infections

Rats !!!

- Recent advances in development of genetically engineered rats

- Likely to see a similar increase in pathogen prevalence



What pathogens are being found in genetically engineered rodents?

- Reemergence of previously recognized pathogens
- Emergence of new pathogens

Postnatal Lung Development

Completed Stage	Mouse/Rat	Human
Alveolar Development	4-7 days	Birth
Capillary Fusion and Septal Thinning	3 weeks	3 years
Alveolar Multiplication	5 weeks	8 years
Lung Growth	6-10 months	20 years

Comparative Respiratory Anatomy/Physiology

	Mouse	Rat	Human
Vomeronasal Organ	Present	Present	Absent
Nasal Turbinates	Double scroll	Double scroll	Simple Scroll
Lung Anatomy	Right: 4 lobes Left: 1 lobe	Right: 4 lobes Left: 1 lobe	Right: 3 lobes Left: 2 lobes
Pleura	Thin	Thin	Thick
Secondary Lobulation	Absent	Absent	Incomplete
Total Lung Capacity (TLC)	~1ml	10 ml	6000 ml
Total Lung (Parenchyma)	18%	24%	12%
Blood-Gas Barrier Thickness	0.32μm	0.38 μm	0.62 μm
Pulmonary Veins	Cardiac muscle	Cardiac muscle	Thin, mainly fibrous wall

Human Pulmonary Disease Models

- Chronic Obstructive Pulmonary Disease (COPD)
  - Emphysema
  - Asthma
- Lung Cancer
- Pulmonary Alveolar Proteinosis (PAP)
- Cystic Fibrosis
- Pulmonary Hypertension
- Pulmonary Fibrogenesis
- Pulmonary Toxicity

Other Considerations

- Seek information on particular strain, genetic modification of animal being examined eg Jackson labs website, pubmed
- Meaning of SPF
- Use of sentinel animals
- Serological screening – Institute of Medical and Veterinary Services (IMVS) in Adelaide

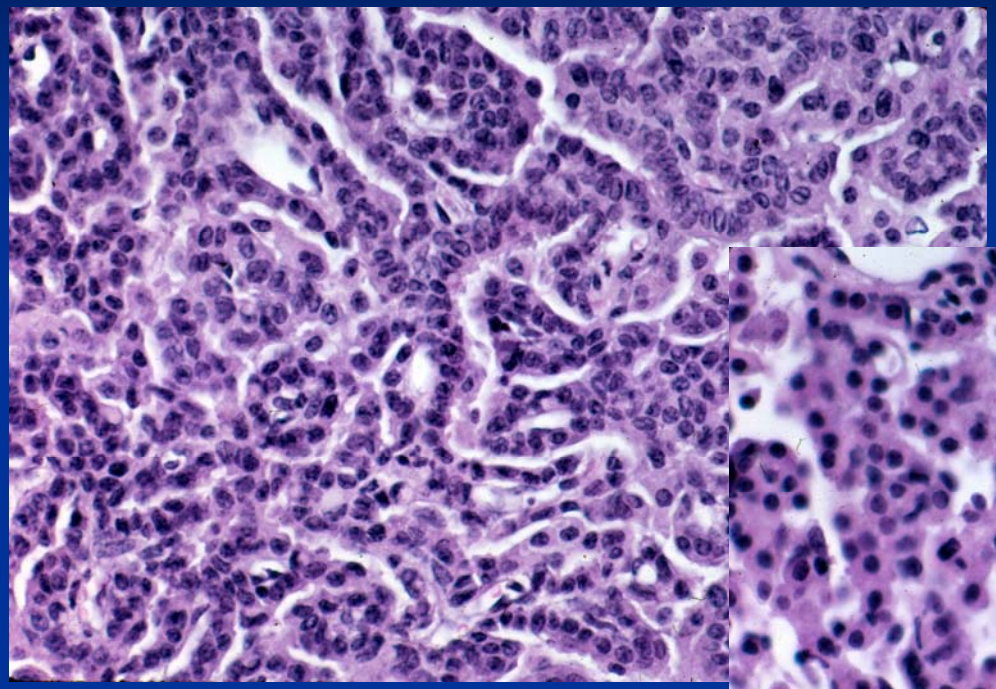
The Laboratory Mouse

- ***Mus domesticus, castaneus, musculus, et al.***
- Normal features
  - Obligate nasal breathers
  - Prominent vomeronasal organs
  - Single left lung lobe, four right lobes.
  - No intrapulmonary bronchi (no cartilage)
  - Cardiac muscle extends around large pulmonary veins

Spontaneous Lesions and Diseases

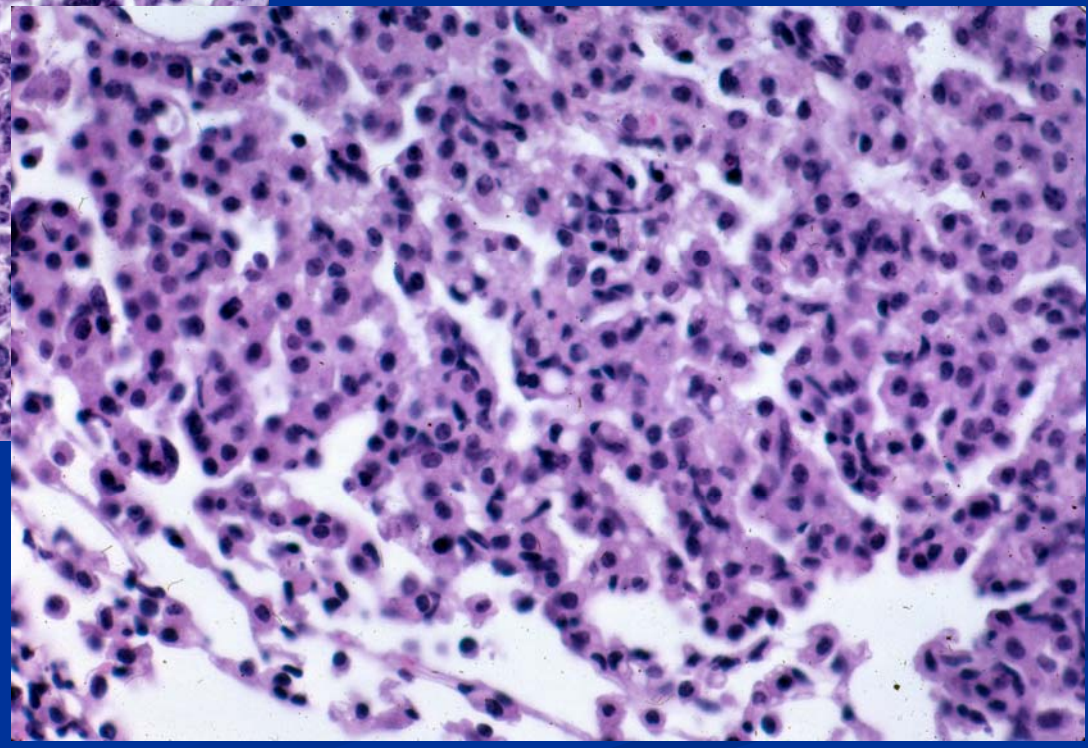
- Most are strain dependent
- Non-infectious lesions
- Neoplastic lesions
  - Bronchoalveolar adenoma or carcinoma
  - T-cell lymphoma
- Infectious diseases

Broncho-alveolar Lung Tumor Types

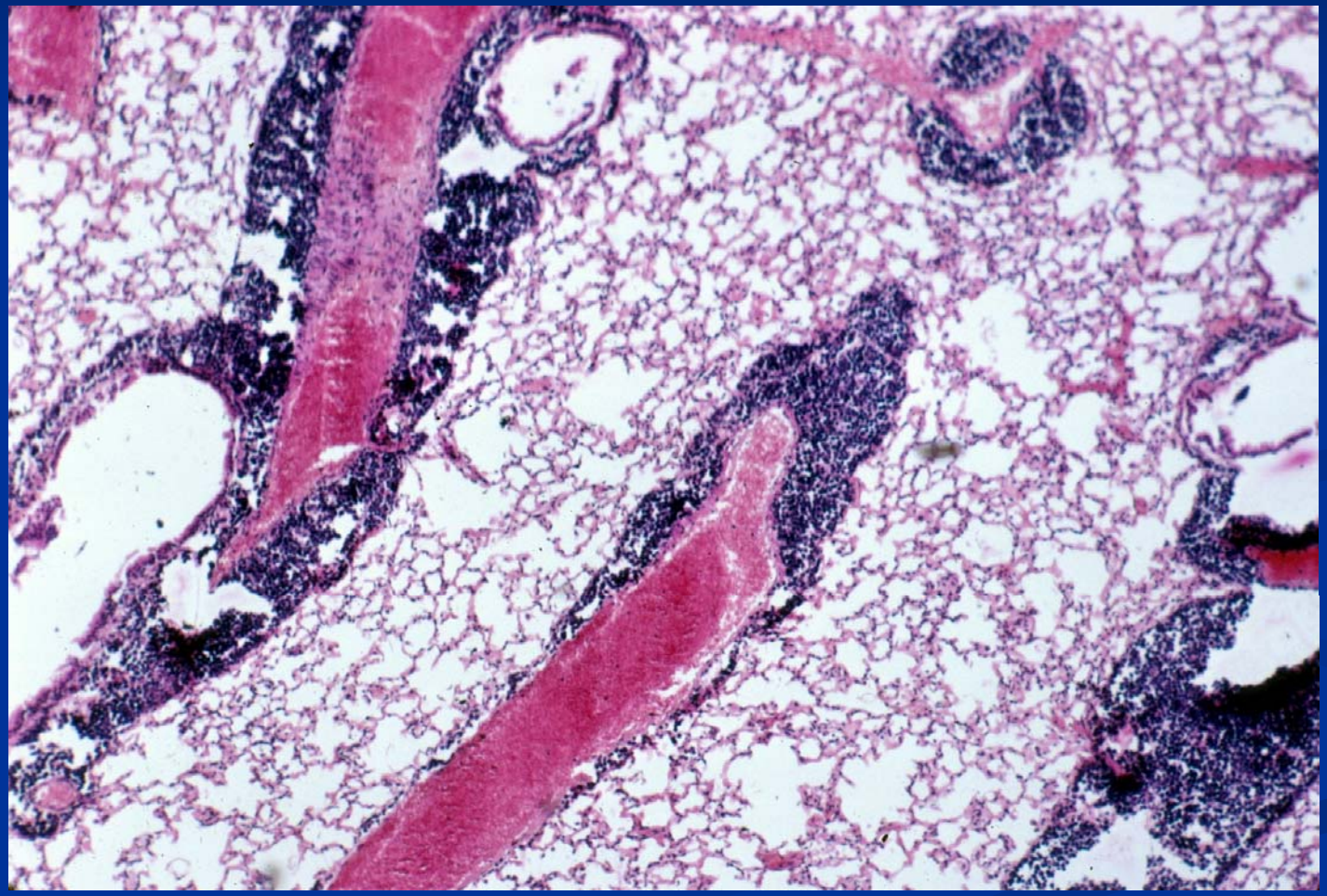


Clara Cell

Type II Cell



T-cell Lymphoma



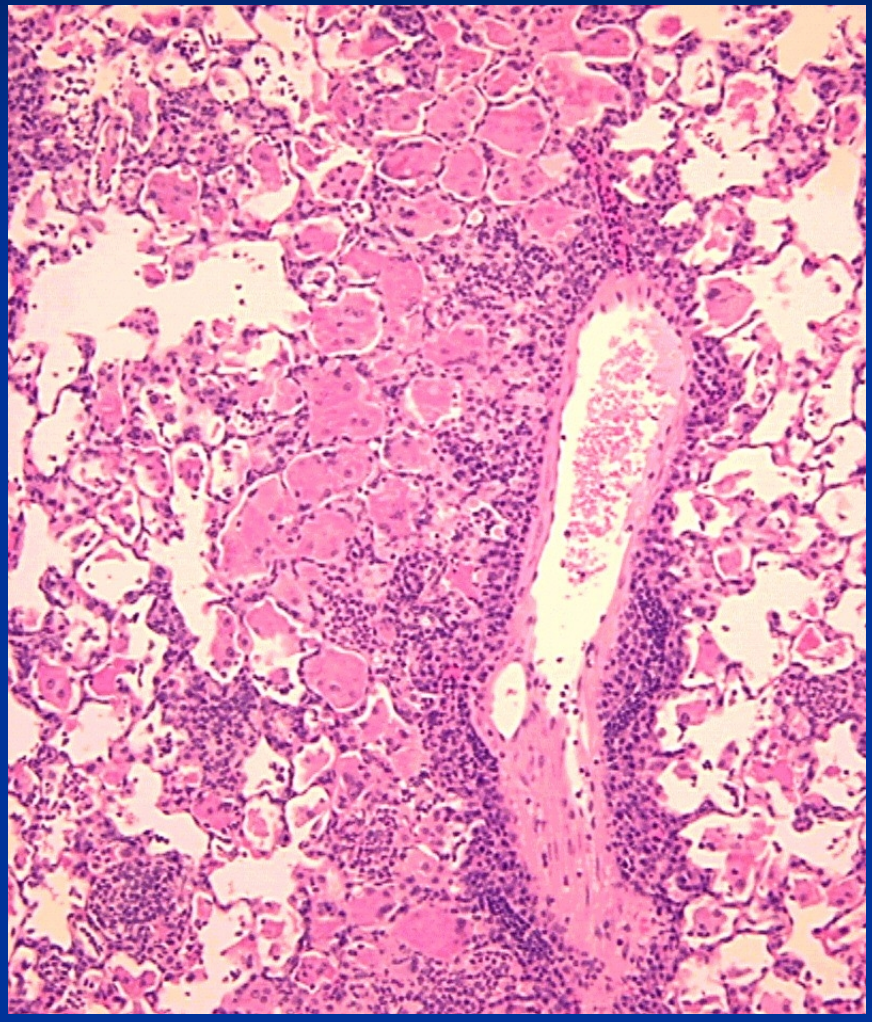
Noninfectious Lesions/Diseases

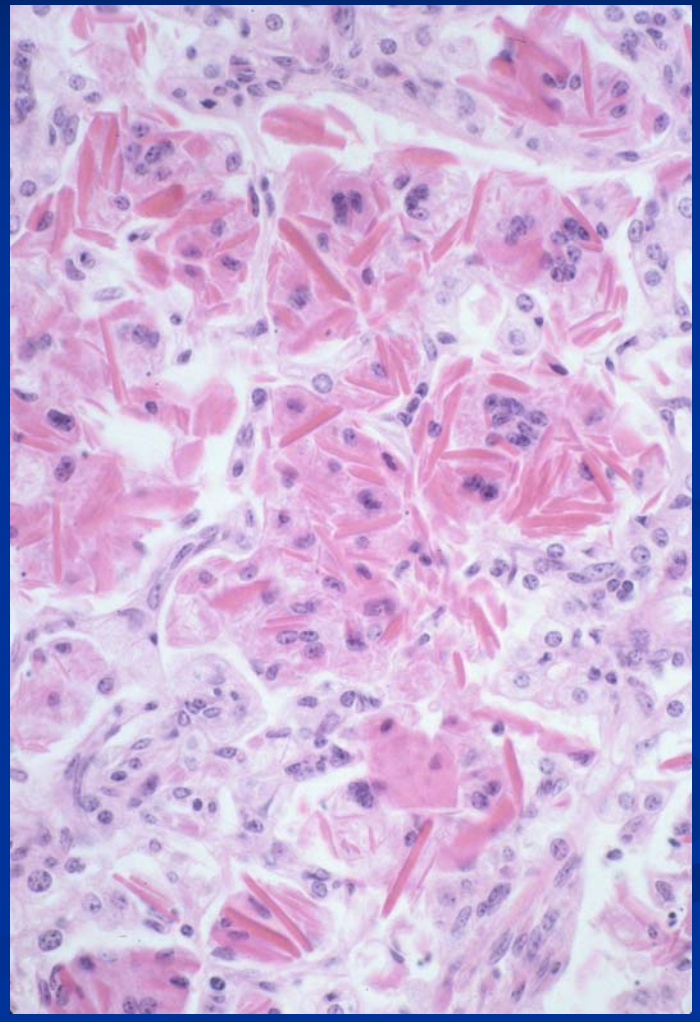
- Eosinophilic secretory inclusions (hyalinosis) in respiratory epithelium (B6, 129) – nasal, etc
- Acidophilic macrophage pneumonia (crystalline inclusions and deposits) in B6, motheaten (B6 mutant) and 129 mice – probably all
- Nasal obstruction - bedding
- Inhalation pneumonia - bedding, food

Acidophilic Macrophage Pneumonia

- Crystals in macrophages, epithelial cells, and alveoli
- Few inflammatory cells
- Somewhat strain specific e.g., 129 strain, moth eaten mice, and GEMS on 129 background.
- Crystals form endogenously - Ym1 (T-lymphocyte derived eosinophil chemotactic factor)
- Crystals also in nose, liver, stomach, and pancreas

Acidophilic Macrophage Pneumonia

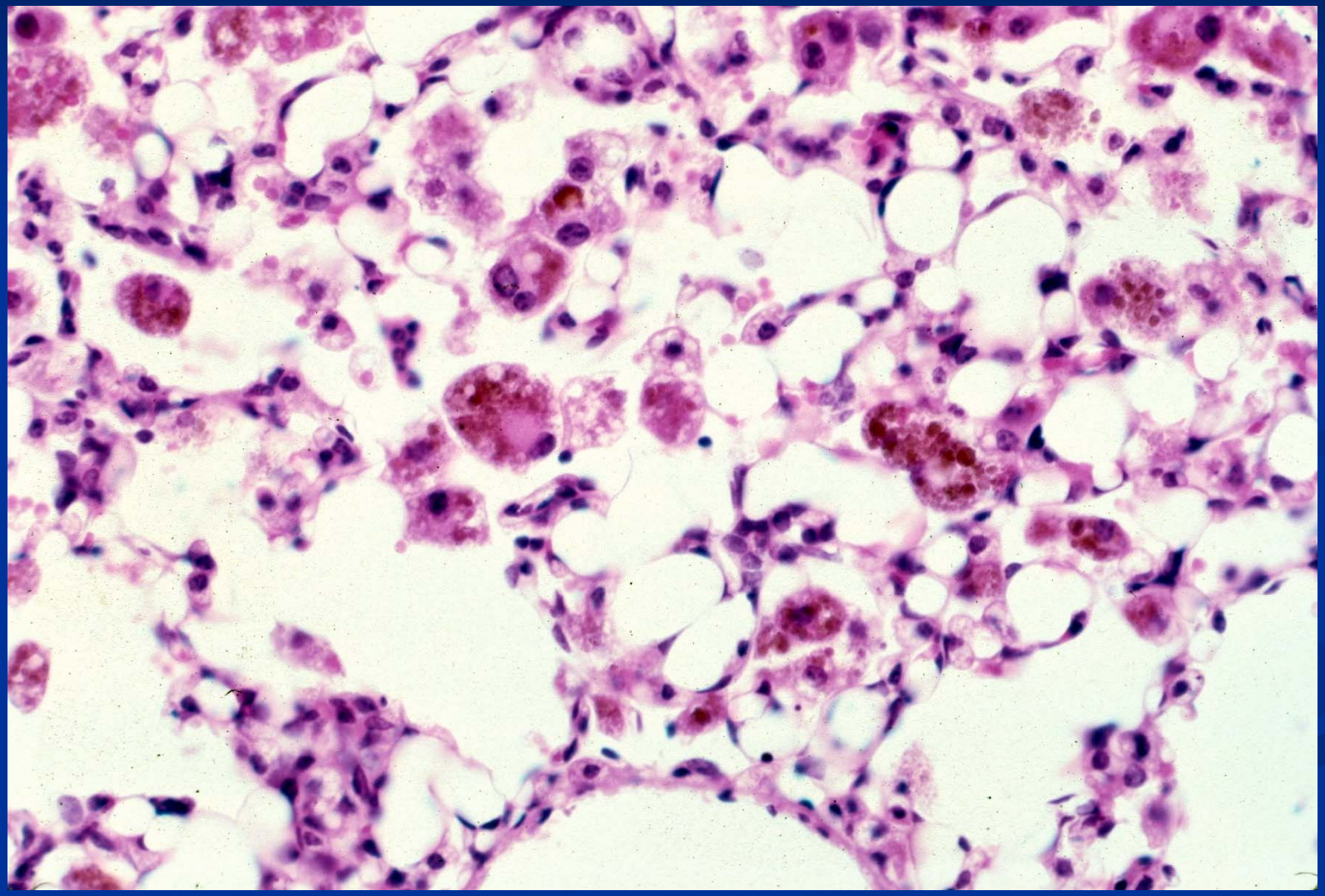




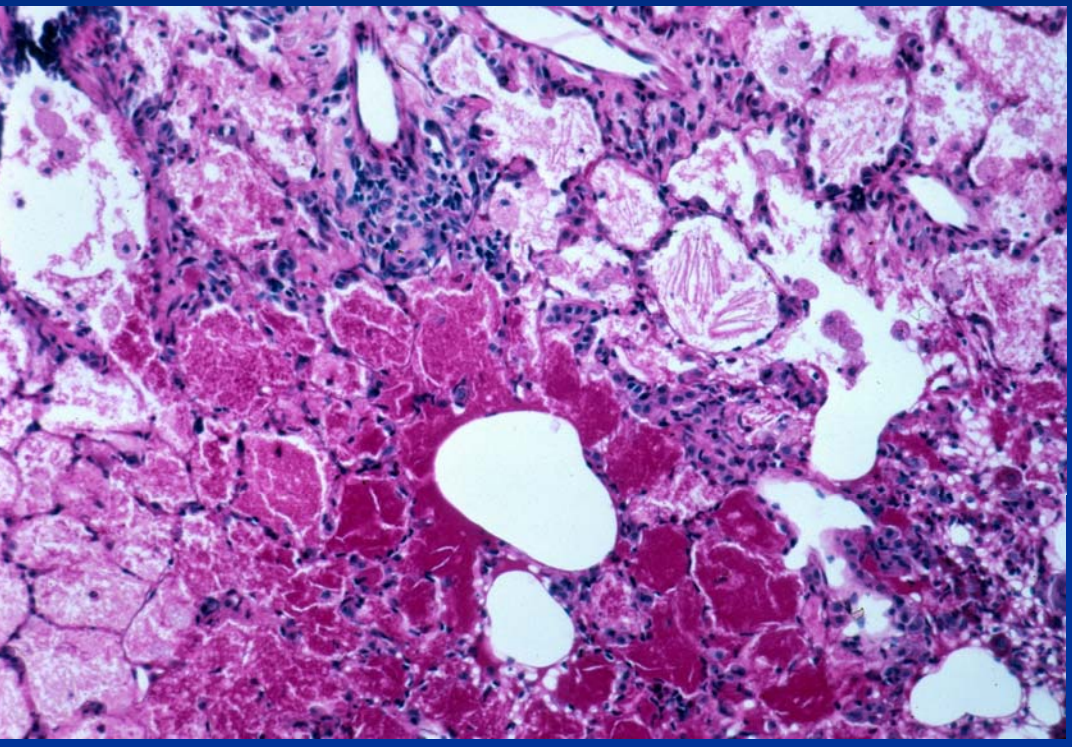
Non-infectious Lesions

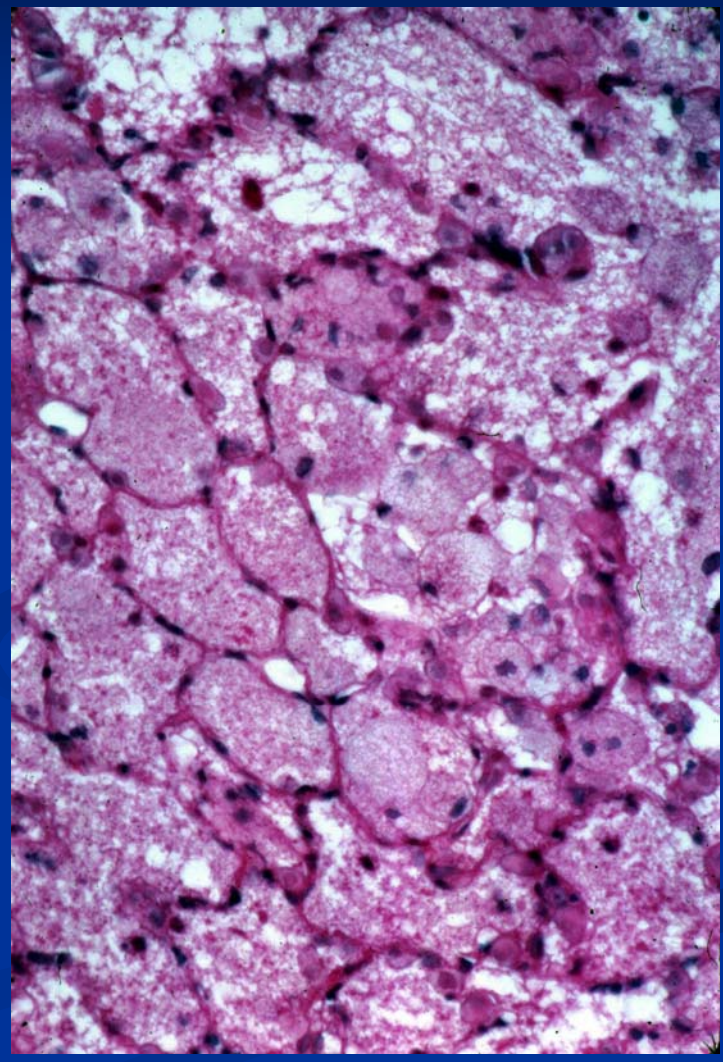
- Alveolar lipoproteinosis/proteinosis
- Alveolar emphysema/Enlarged air spaces
- Psommoma bodies/Alveolar microlithiasis (adult mutant *nackt* mice)
- Senile amyloidosis (SAM1 mice, Apoa2c allele)
- Lymphoid foci
- Chronic passive congestion
- Intraalveolar pigmented macrophages
- Alveolar histiocytosis

Chronic Passive Congestion



Secondary PAP





Infectious Diseases

- Viral
  - Paramyxoviruses
    - Pneumonia virus of mice (PVM)
    - Sendai virus
- Bacterial
  - CAR bacillus
  - *Mycoplasma pulmonis*
  - *Pasteurella pneumotropica*
  - *Pseudomonas aeruginosa*
  - *Staphylococcus aureus*
- Mycotic
  - *Pneumocystis carinii*

Pneumonia Virus of Mice (PVM) – Now Murine Pneumonia Virus (MPV)

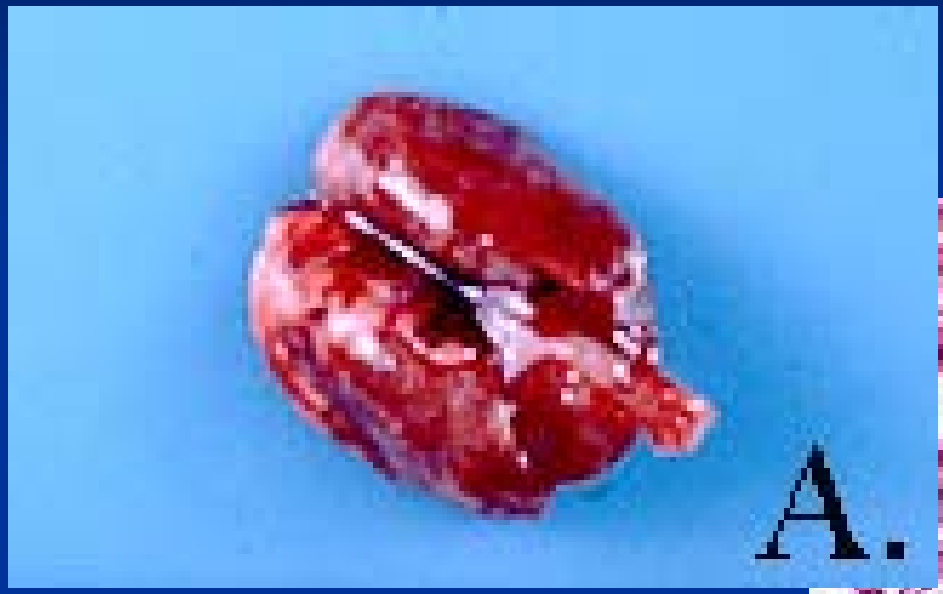
- Prevalence: common
- Virus targets respiratory epithelial cells and type 2 pneumocytes
- Diagnosis: serology; lesions in immunodeficient mice
- Disease: subclinical upper respiratory infection
- Lesions: Nude and SCID mice develop wasting disease due to progressive bronchointerstitial pneumonia
- Transmission: respiratory
- Duration: acute (except immunodeficient mice)
- Renamed PVM to MPV (murine pneumonia virus) – a pneumovirus (Family Paramyxoviridae)

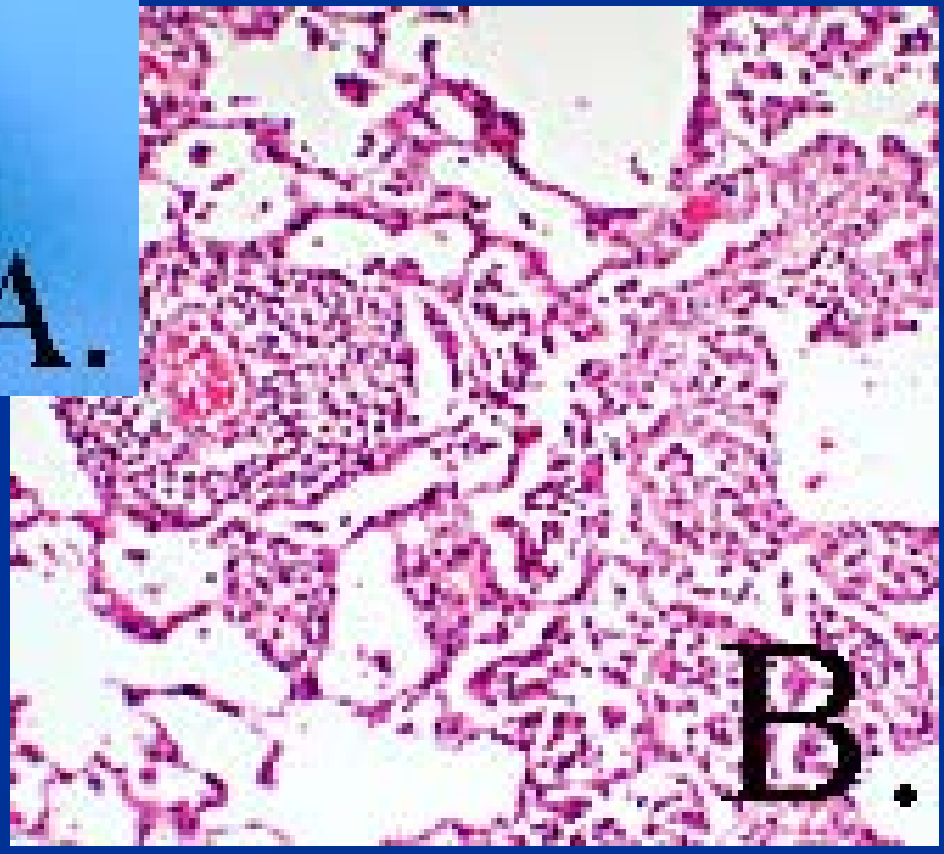
Sendai Virus (SeV)

Respirovirus, Family Paramyxoviridae

- Prevalence: recently common, but now rare in US.
- Diagnosis: serology, lesions
- Disease: most clinically significant virus infection -clinical disease in immunocompetent mice of all ages
- Lesions: necrotizing rhinitis, tracheobronchitis, bronchointerstitial pneumonia.
  - Recovery phase – hyperplasia, squamous metaplasia, fibrosis
  - Athymic and SCID mice: proliferative (rather than necrotizing) bronchiolitis and interstitial pneumonia.
- Target cells: respiratory epithelium and type 2 pneumocytes
- Transmission: respiratory/aerosol
- Duration: acute (except immunodeficient mice)

Sendai Virus





Bacterial Disease Agents

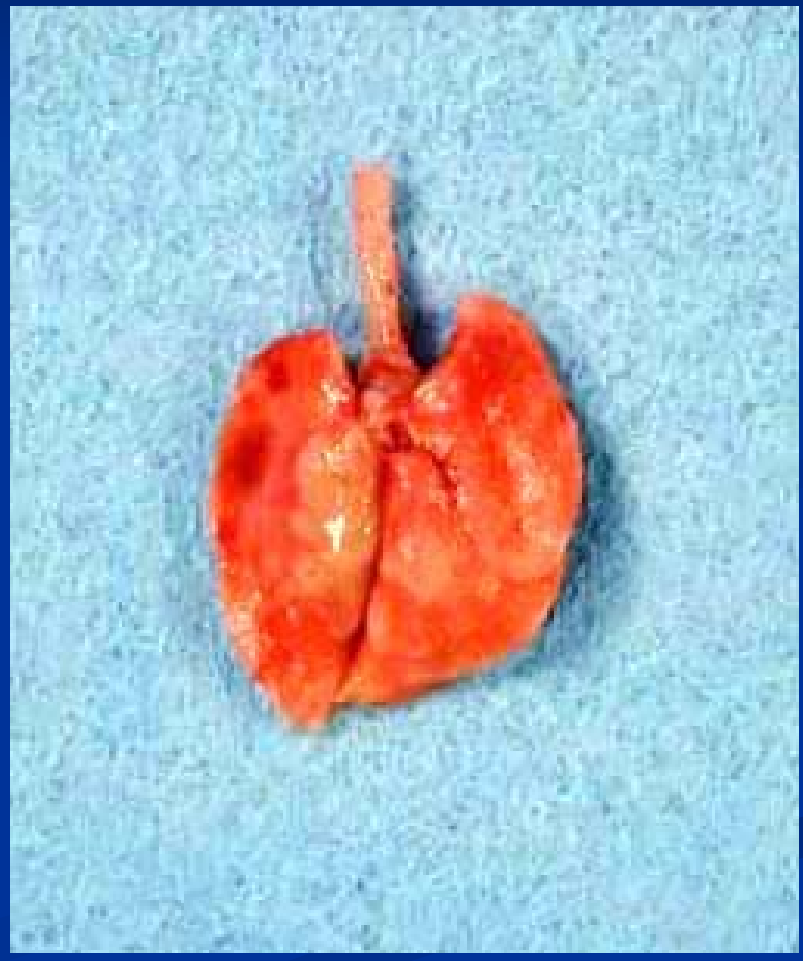
- *Mycoplasma spp.*
- *Pasteurella pneumotropica*
- Cilia-Associated Respiratory (CAR) Bacillus
- *Corynebacterium kutscheri*
- *Mycobacterium avium-intracellulare*
- *Chlamydophila psittaci*

Chronic Respiratory Disease of Mice

- *Mycoplasma pulmonis* often in concert with other agents (Sendai virus, CAR bacillus, etc.)
- Other factors: high ammonia

Chronic Respiratory Disease

- Lesions
  - Chronic bronchopneumonia
  - Peribronchiolar lymphoplasmacytic infiltrates
  - May also have rhinitis and otitis



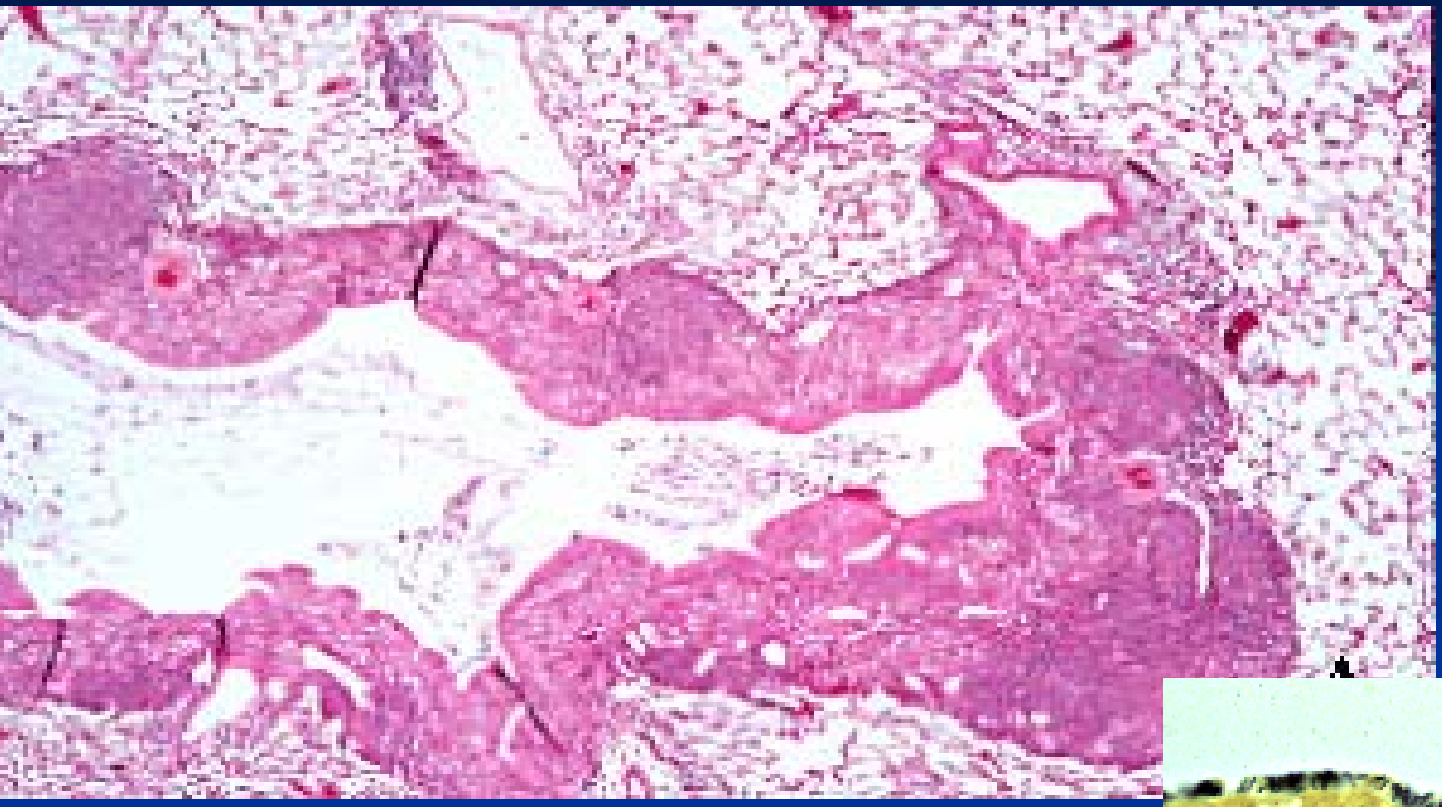
Mycoplasmosis

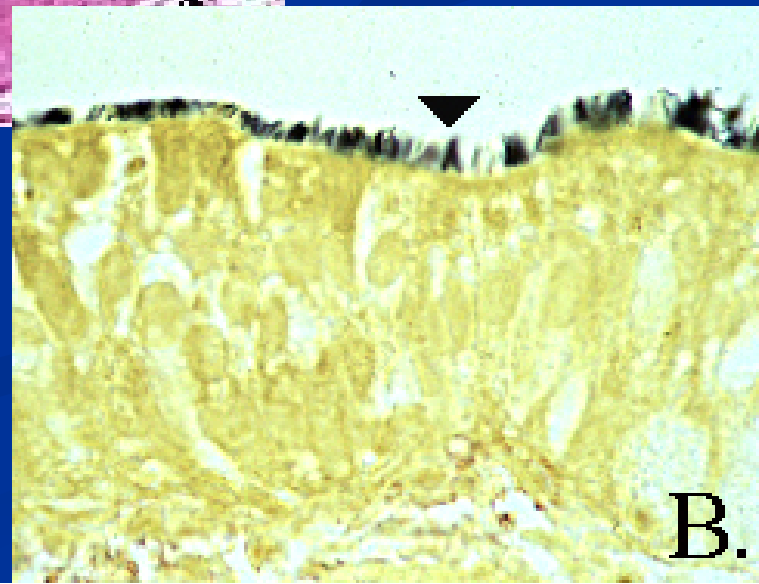
- Prevalence: *M. pulmonis* moderate. *M. arthritidis* less common and others rare or nonexistent.
- Diagnosis: culture, serology, lesions (if present).
- Disease: often subclinical but major role in chronic respiratory disease
- Lesions: chronic suppurative rhinitis, otitis and bronchopneumonia
- Transmission: respiratory, other
- Duration: chronic

Cilia-Associated Respiratory (CAR) Bacillus

- Prevalence: common
- Diagnosis: serology available, PCR use increasing.
- Histology: with silver stain, organisms among cilia
- Disease and lesions: often part of chronic respiratory disease - none to chronic suppurative pneumonia.
- Transmission: direct contact
- Duration: chronic
- Comment: Rats, rabbits, pigs, humans also infected, but antigenically diverse members –
  - Related to *Flexibacter* and *Flavobacterium spp.*

CAR Bacillus Infection





Corynebacterium kutscheri (Pseudotuberculosis)

- *Prevalence:* rare (once common)
- *Diagnosis*: culture, Gram stain of lesions, serology (not used)
- *Disease*: Caseopurulent abscesses in liver, kidney, lung and other sites. Subclinical carrier state common..
- *Transmission:* direct contact
- *Duration:* chronic, but probably not latent

Pasteurella pneumotropica

- Prevalence: high prevalence of infection, sporadic disease
- Diagnosis: culture, lesions
- Disease: opportunistic organism – part of normal microflora in nasopharynx and gut
  - Conjunctivitis, ophthalmitis, periorbital abscesses, otitis, pneumonia, cystitis, prepucial gland and subcutaneous abscesses, pyometra, etc. Dermatitis in nude mice.
- Transmission: normal flora
- Duration: chronic
- Comment: emerging disease - suppurative bronchopneumonia in partially immunodeficient mice co-infected with *Pneumocystis murina*.

Pasteurellosis - Conjunctivitis

Other Infectious Agents

- Fungi
  - *Aspergillus sp.*- infrequent, but may be in outbreak form
  - *Pneumocystis murina* - IMPORTANT
- Parasites
  - *Toxoplasma gondii* - rare

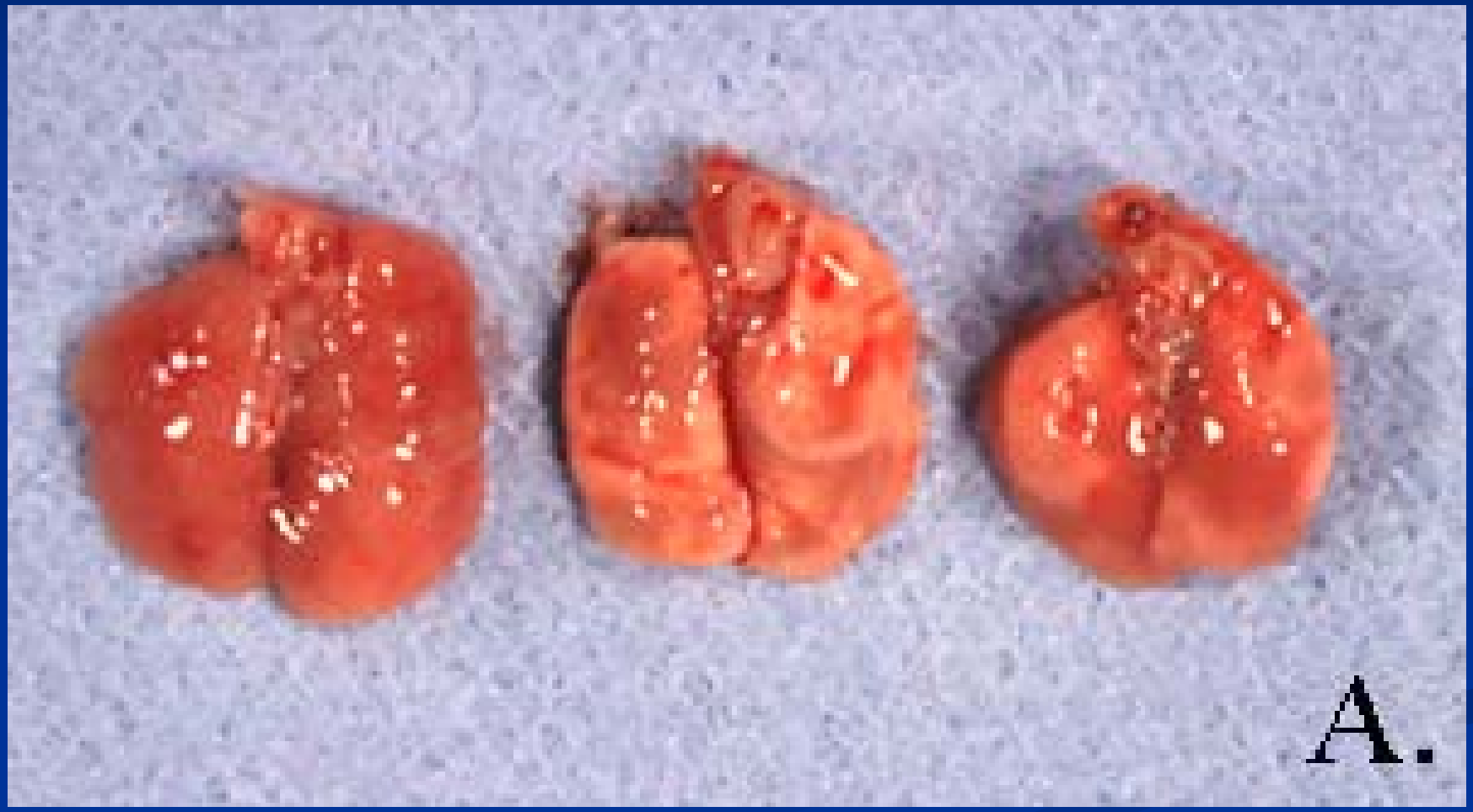
Aspergillus sp

- Prevalence: rare disease
- Diagnosis: lesions, culture
- Disease: pulmonary granulomas due to *Aspergillus terreus* in immunodeficient genetically altered mice (gp91 phox null) maintained on corncob bedding.
- Transmission: inhalation from contaminated corncob bedding
- Duration: chronic
- Comment: opportunistic fungus

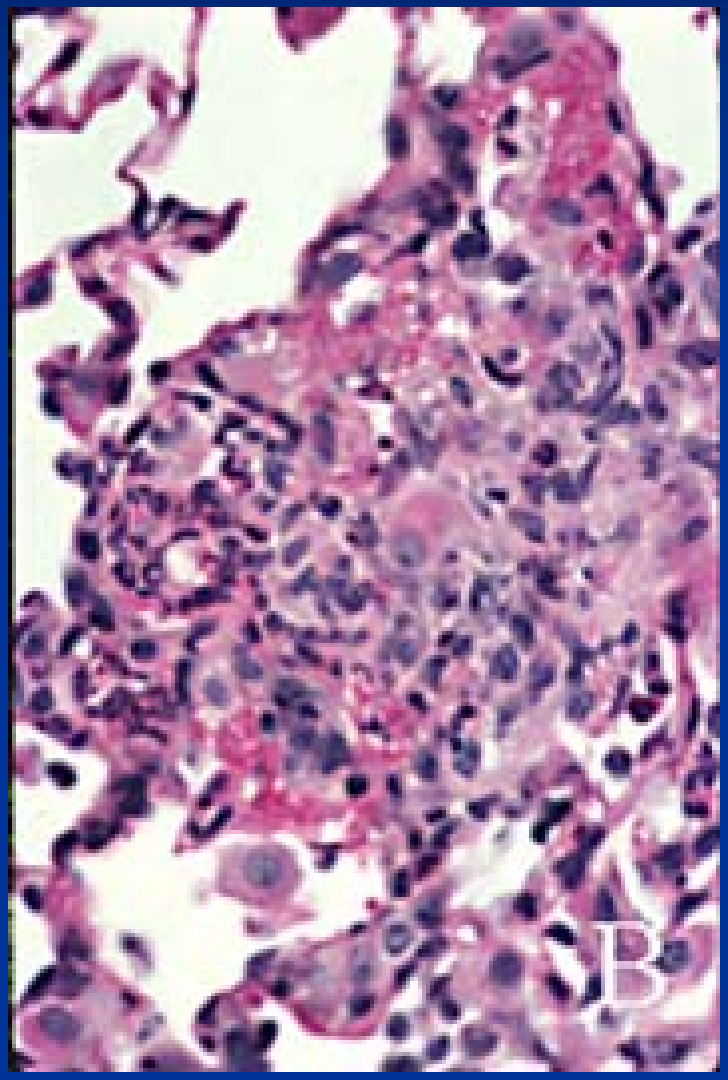
Pneumocystis murina sp. nov

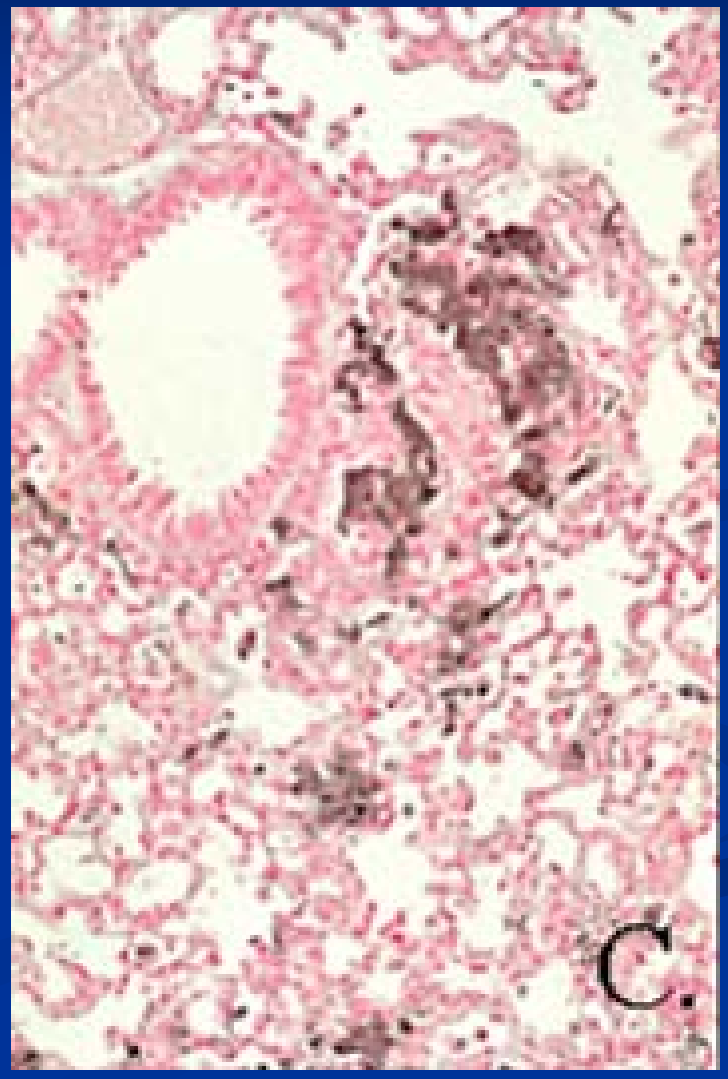
- Prevalence: high rate infection; disease rate low, except in immunodeficient mice
- Diagnosis: silver stain of organisms (differentiate from debris in macrophages) in histopath sections, may need PCR
- Disease: serious if immunologically deficient/steroids/low protein diet
- Lesion: lungs firm, pale, mottled and do not collapse – same as other species
- Histopathology: granular material in alveoli
- Transmission: contact aerosol. Immunocompetents as carriers
- Duration: chronic
- Mouse, rat, human *Pneumocystis* sp differ genetically, based upon 18S rRNA gene sequence. Human agent is now *P. jirovecii*; rat agents are *P. carinii* and *P. wakefieldiae*.

Pneumocystis muris



Pneumocystis muris (H& E, silver stain)





Toxoplasma gondii

- Prevalence: rare
- Diagnosis: histology, PAS-positive organisma in muscle and heart.
- Disease: usually subclinical.
- Lesions: interstitial pneumonia with involvement of other organs
- Transmission: orofecal (cat feces containing oocysts). Also cannibalism and vertical (in utero) transmission.
- Duration: chronic

Current Important Mouse Diseases

- Pneumocystosis – discussed above
- Helicobacter infection
  - Hepatic necrosis and inflammation
  - Enteritis and especially proliferative enteritis
  - Diagnosis by PCR
  - Role in hepatic carcinogenesis
- Mouse hepatitis virus

The Laboratory Rat

- Obligate nasal breathers
- Prominent vomeronasal organs
- Single left pulmonary lobe, four right lobes
- No intrapulmonary bronchi
- Cardiac muscle extends around large pulmonary vessels
- Serous cells in respiratory epithelium (unique to rat)

Spontaneous Noninfectious Disease

- Alveolar histiocytosis
- Inhalation pneumonia - bedding, food
- Neoplasia
  - Large granular cell leukemia: NK cells. F344, WAG strains. Splenomegaly with infiltration of lung, liver, lymph nodes
  - Primary pulmonary neoplasms rare -bronchiolo-alveolar adenoma/carcinoma

Spontaneous Noninfectious Disease of Old Rats

- Rhinitis
- Mineralization of tracheal cartilage- focal or multifocal.
- Eosinophilic perivascular infiltrates
- Mineralization of pulmonary arteries
- Hair shaft emboli in intravenous injection studies

Viral Diseases

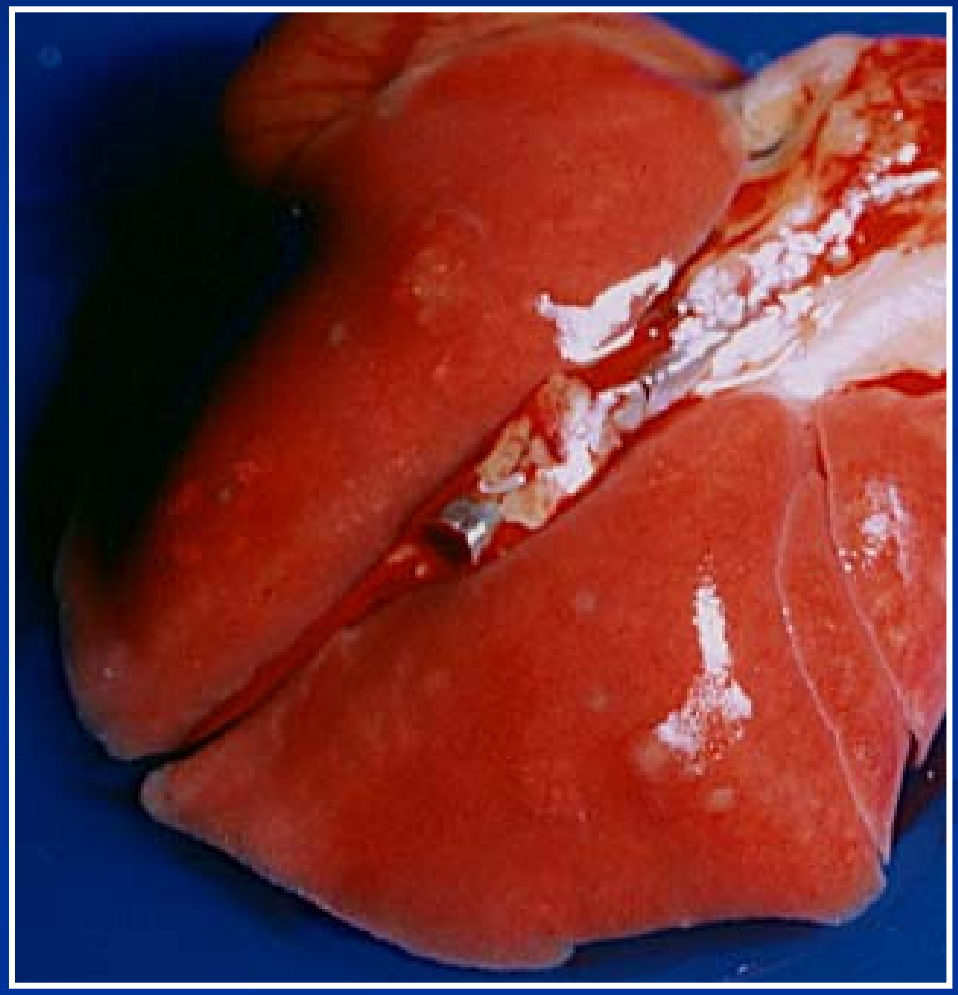
- Mainly similar to mice
  - Sendai virus
  - Murine pneumonia virus (MPV) - more apt to produce lung lesions in naturally infected rats than mice.
- Additional viral agents
  - Rat corona viruses – similar to MPV – but necrotizing upper and lower respiratory lesions with interstitial pneumonia and sialodacryoadenitis.
  - Hantavirus

Hanta virus

- Prevalence: rare in laboratory rats, common in Norway rats
- Diagnosis: serology
- Disease: none reported in rats, but infection chronic
- Transmission: urine, saliva, respiratory
- Comment: zoonotic
  - Asian isolates - hemorrhage fever with renal syndrome in humans.
  - American strains - acute pulmonary disease in humans. *Peromyscus spp.* (white footed mouse) major reservoir host in U.S.

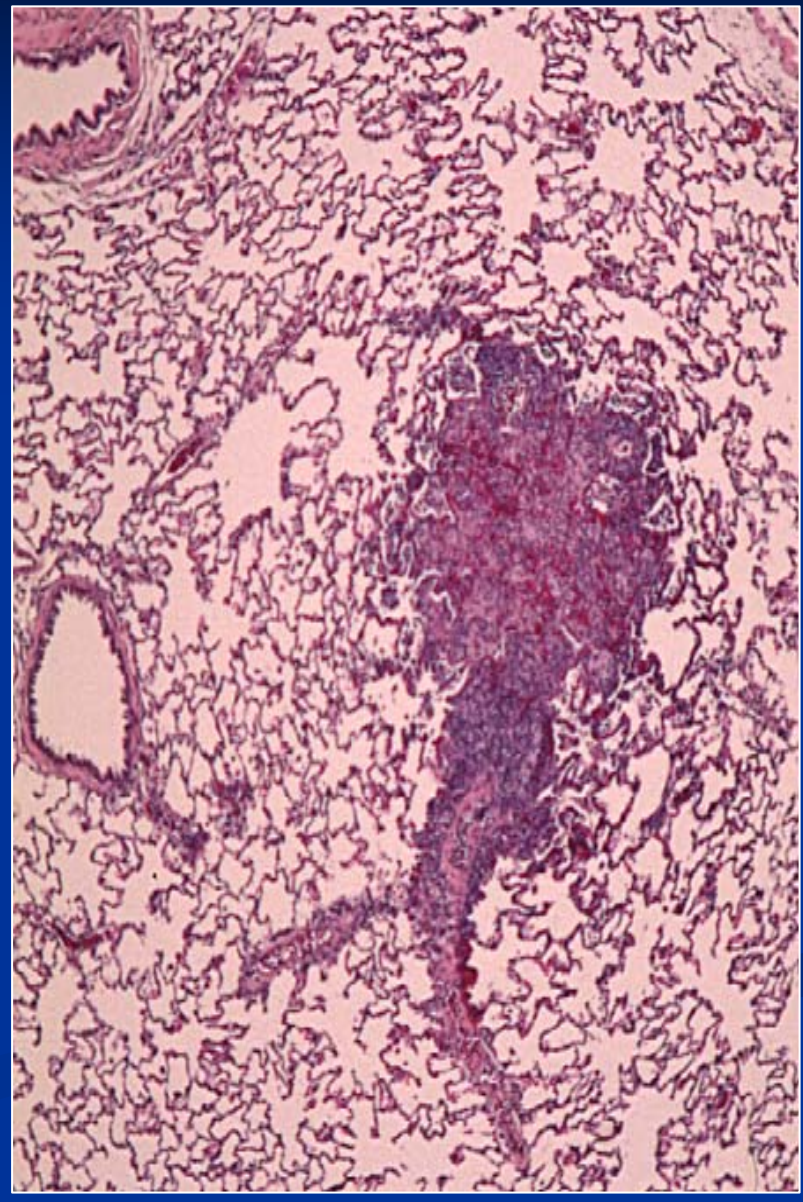
Example of Emerging Pathogen

- Gross lesions
  - Small, raised, focal, grey white lesions
- 6-8 week old
- Sporadic
- Asymptomatic
- Not previously recognized



Rat Respiratory Virus

- Perivascular and parenchymal lesions
- Bronchioles not involved
- ? Hantavirus??
- Complicates respiratory models



Bacteria

Mycoplasma spp. (as mice)
Bordetella bronchiseptica
Cilia-Associated Respiratory (CAR) Bacillus (as mice)
Corynebacterium kutscheri (as mice)
Hemophilus spp.
Klebsiella pneumoniae
Pasteurella pneumotropica (as mice)
Pseudomonas aeruginosa
Staphylococcus spp.
Streptobacillus moniliformis
Streptococcus pneumoniae
Streptococcus spp.

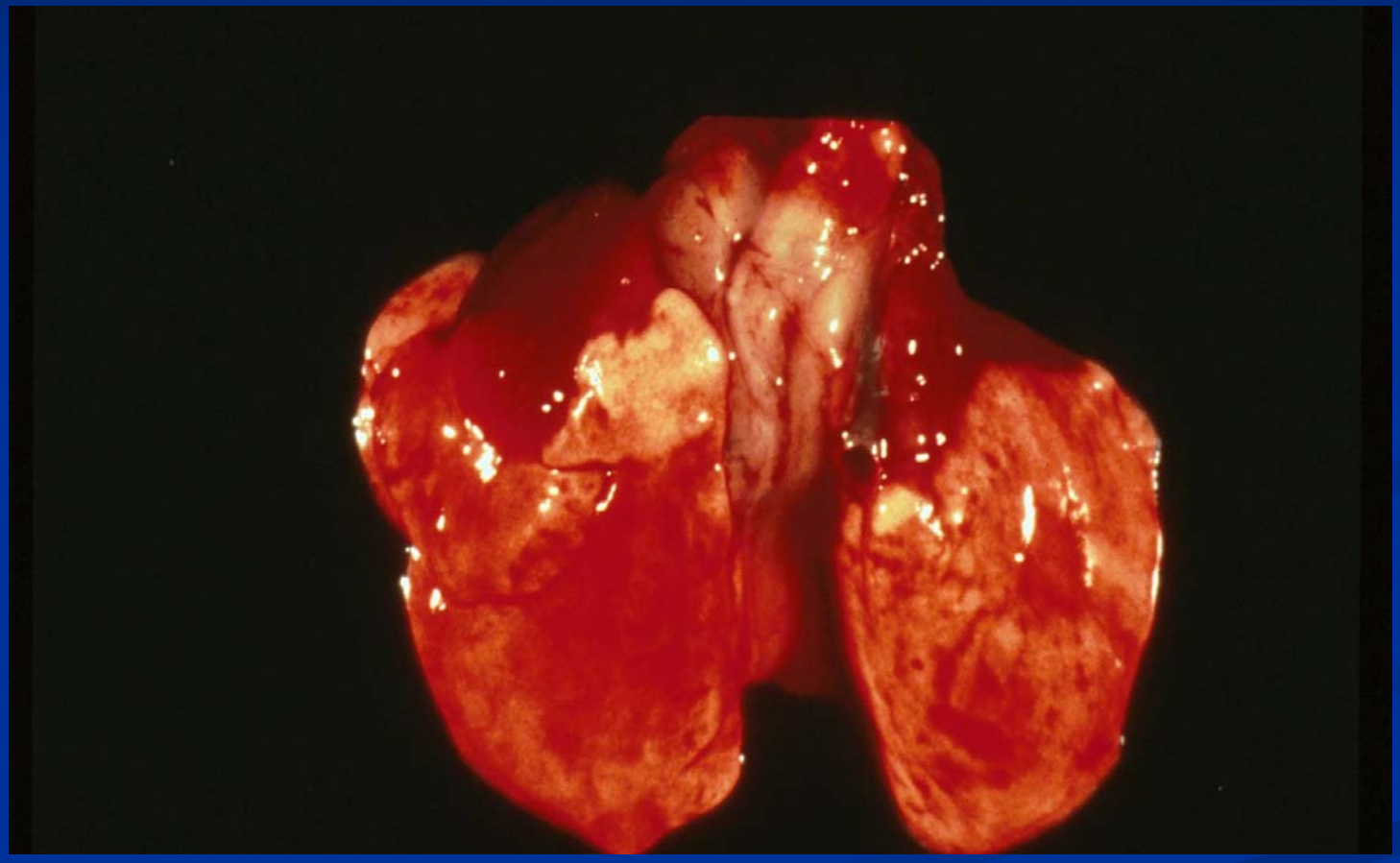
Chronic Respiratory Disease

- Similar to mice
- Usually involvement of multiple bacterial agents
- *Mycoplasma pulmonis* usually involved
- Predisposition by viruses, ammonia

Murine respiratory mycoplasmosis (*Mycoplasma pulmonis*)

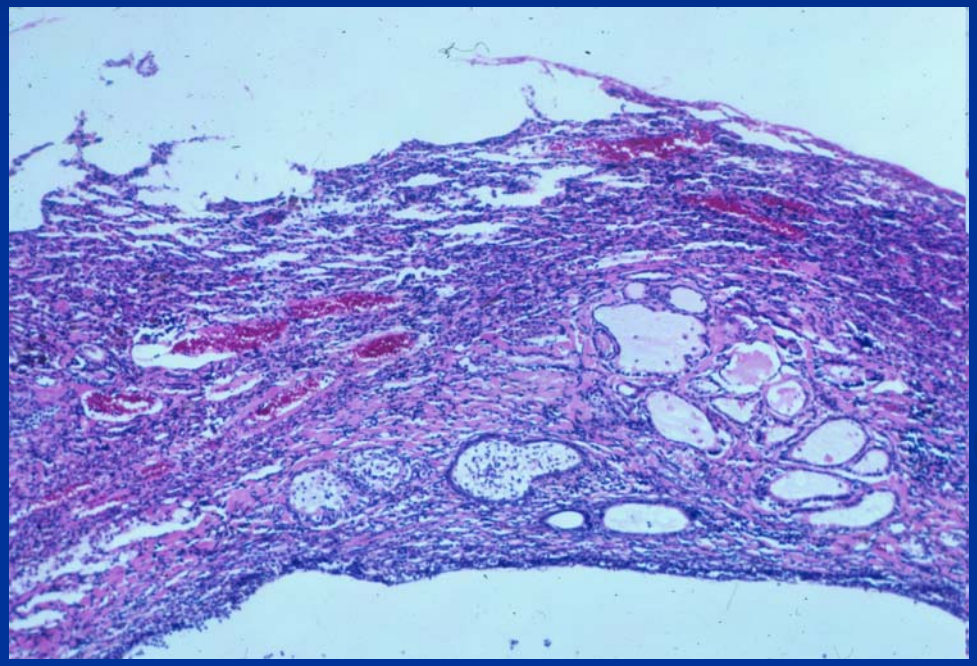
- Synonym: chronic respiratory disease (CRD)
- Was most significant spontaneous lesion in most rat colonies.
- Principally an upper respiratory tract pathogen.
- Severe lung lesions common only in advanced cases
- Earliest lesions in nares, larynx, and middle ear.
- Lung involvement
  - Lymphoid hyperplasia and infiltration lymphoid tissue.
  - Bronchiectasis in advanced lesions

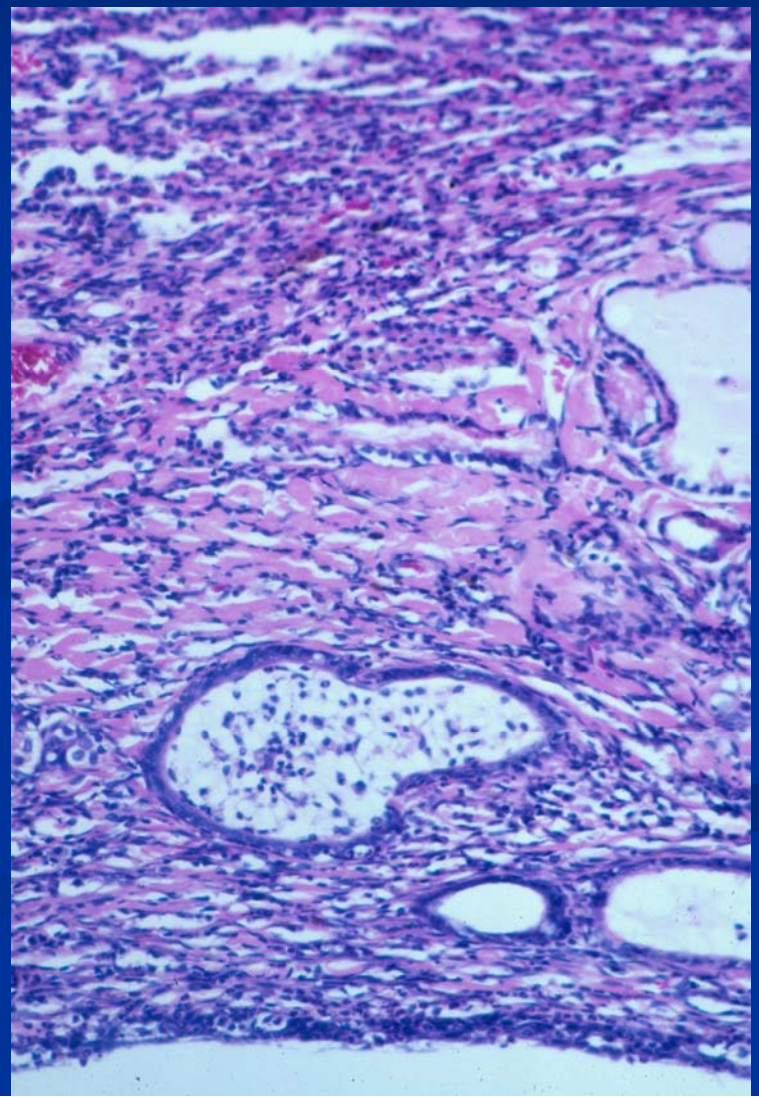
Mycoplasmosis



Chronic Respiratory Disease

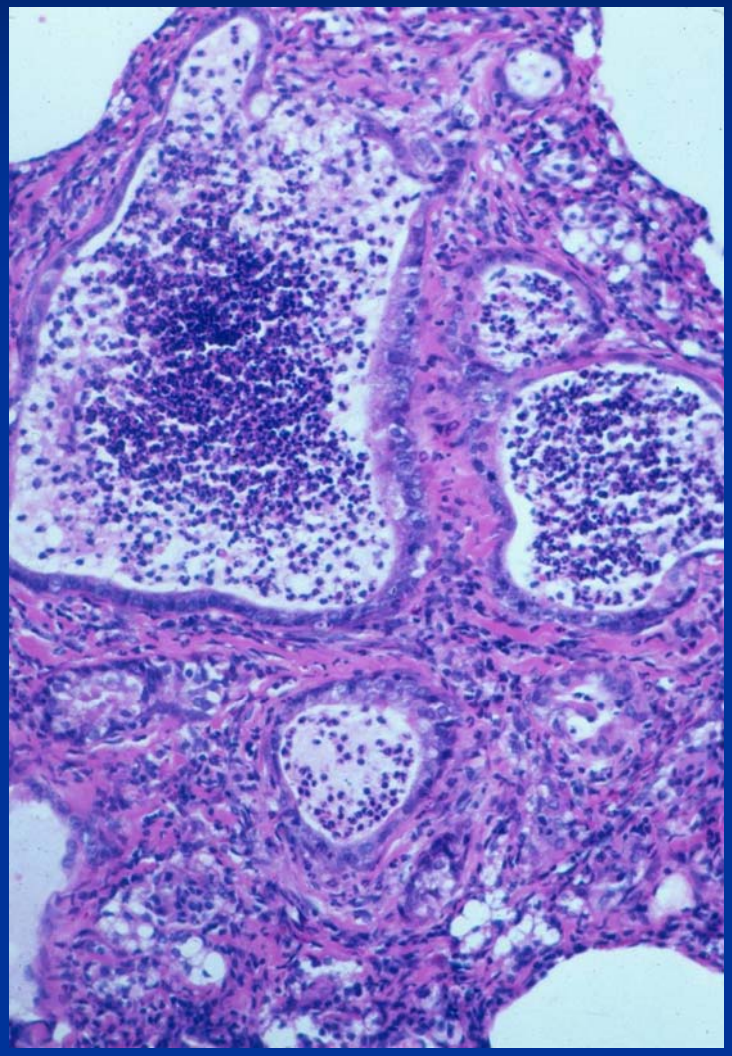
Fibrosis, Chronic Inflammation

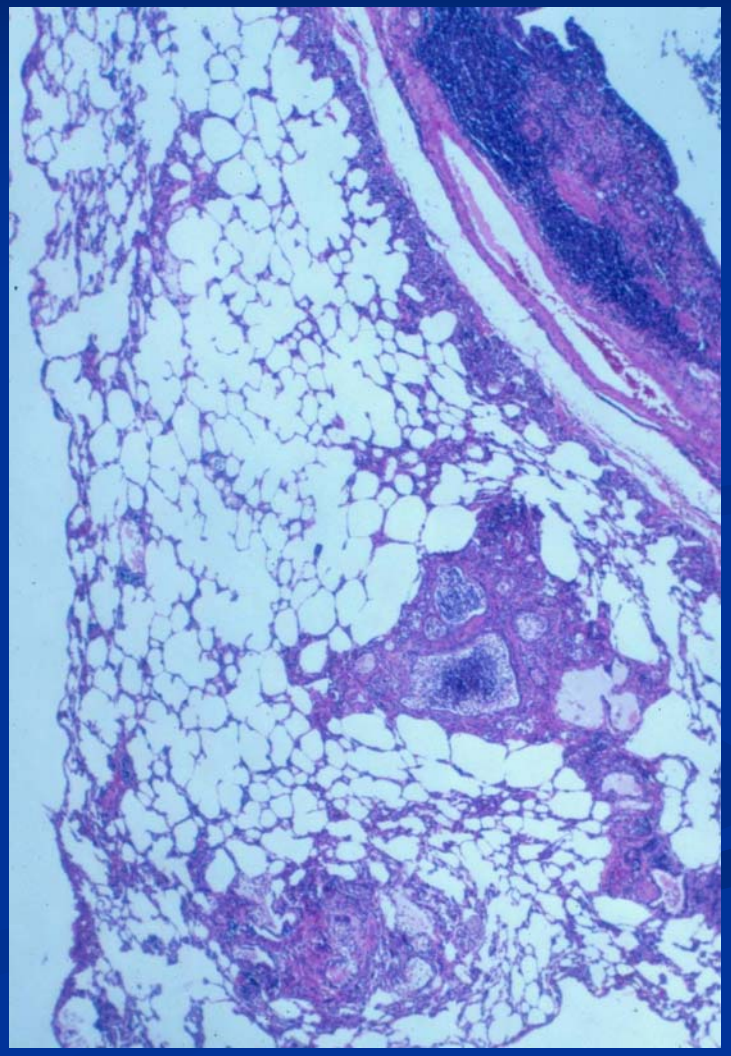




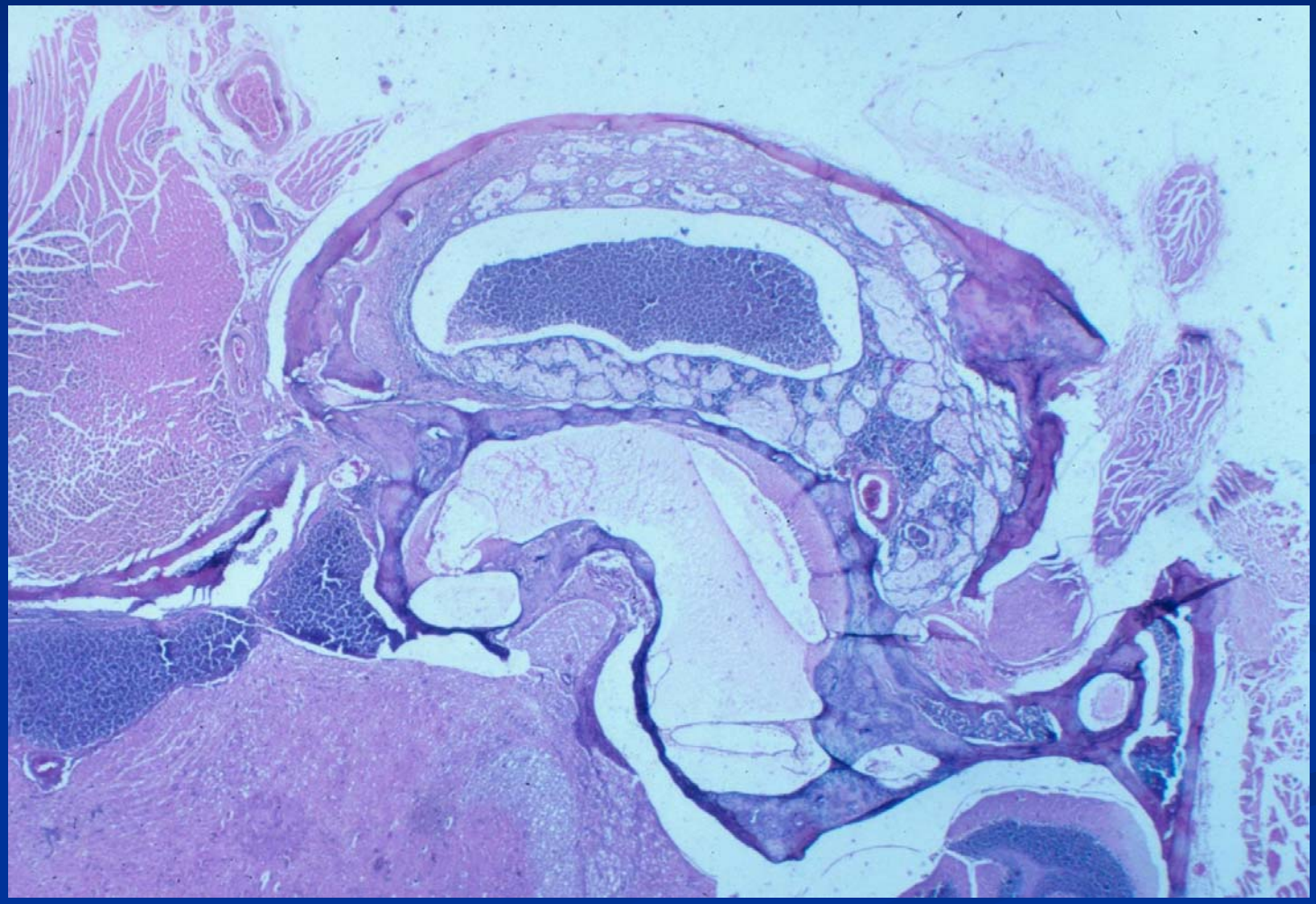
Chronic Respiratory Disease

Fibrosis, Lymphoid Infiltrates



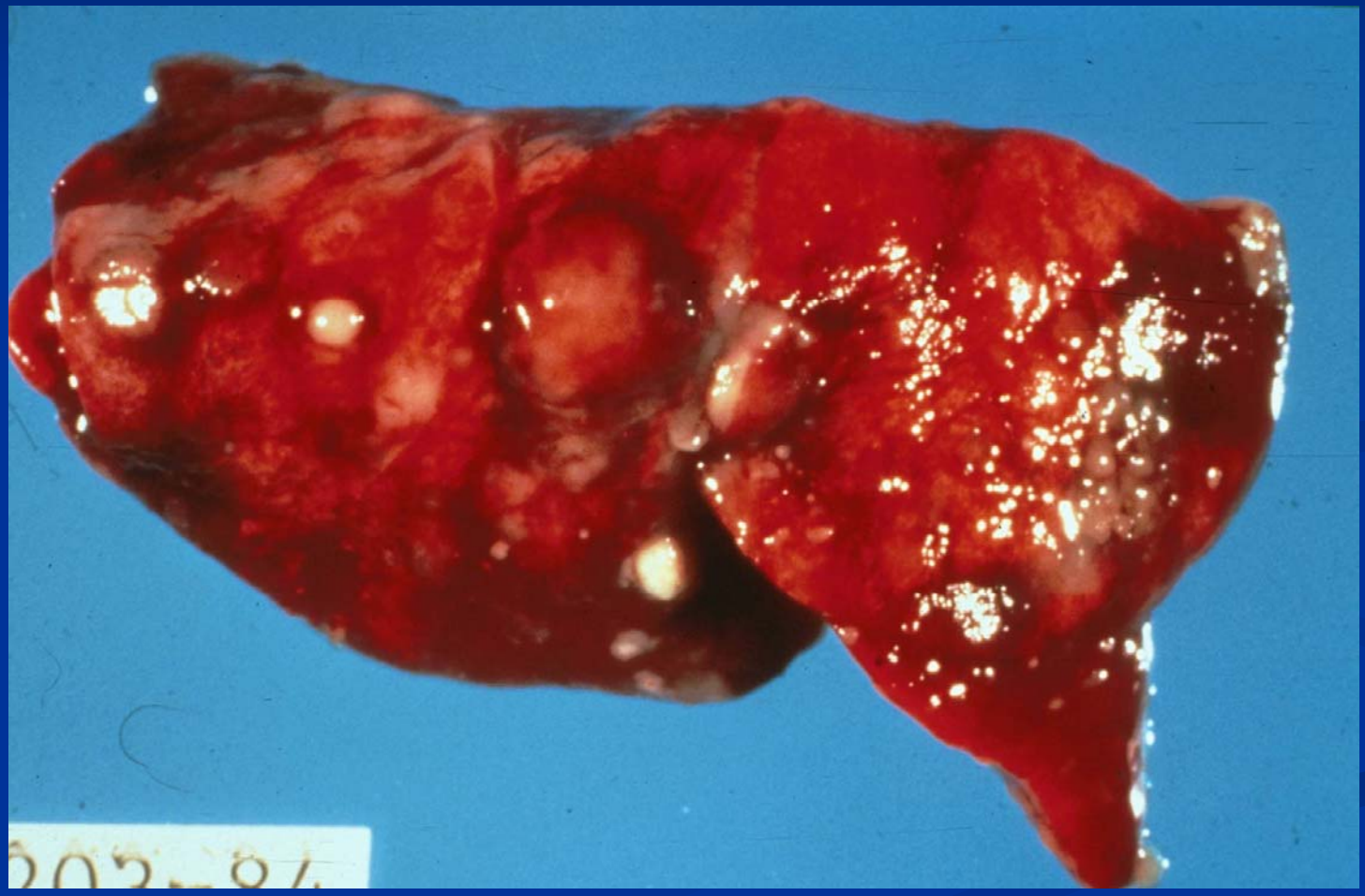


Mycoplasma Otitis



Corynebacterium kutscheri—Rat

Lung abscesses and pneumonia



Streptococcus pneumoniae (Diplococcus, Pneumococcus)

- *Prevalence:* low, can see outbreaks of disease
- *Diagnosis:* culture lesions, Gram stain exudate
- *Disease:* subclinical carriers common (80 %).
- *Lesions:* rhinitis, fibrinopurulent pleuritis, pericarditis, peritonitis, periorchitis, meningitis, otitis and pneumonia.
- *Transmission:* respiratory, contact
- *Duration:* chronic carriers/acute disease
- *Comment:* pathogenicity varies with serotype.

Other Infectious Agents

- Fungal – similar to mice
  - ***Pneumocystis carinii***
  - ***Pneumocystis wakefieldii***
- Parasitic
  - ***Trichosomoides crassicauda*** **(bladder thread worm)**

Trichosomoides crassicauda (bladder thread worm)

- *Prevalence:* infrequent
- *Diagnosis:* bipolar ova in urine, worms in bladder, ureters and renal pelves
- *Disease:* eggs hatch, penetrate stomach wall, migrate through lungs and other viscera and seek urinary tract epithelium.
- Pathology: migrating larvae incite eosinophilia and granulomata, especially in lungs.
- *Transmission:* urine.

Respiratory Diseases of Rabbits

- Order Lagomorpha
- There are over 100 different breeds - descendants of European wild rabbit, *Oryctolagus cuniculus*
- Majority used in biomedical research are New Zealand white
- Heterophils rather than neutrophils
- Anatomic feature - thick medial walls of pulmonary vessels

Viral Respiratory Diseases

- **Rare, expect as part of systemic disease**
- **Rabbit Calicivirus -** hemorrhages in lung from coagulopathy (tracheal hyperemia).
- **Myxomatosis** – poxvirus – can affect lung
- **Rabbit pox - o**rthopoxvirus
- Papular lesions in oropharynx and respiratory tract, focal necrosis with leukocyte infiltration.
- **Herpesvirus sylvilagus**
- Interstitial pneumonia with prominent lymphoid hyperplasia in the lung.

Bacterial Respiratory Diseases

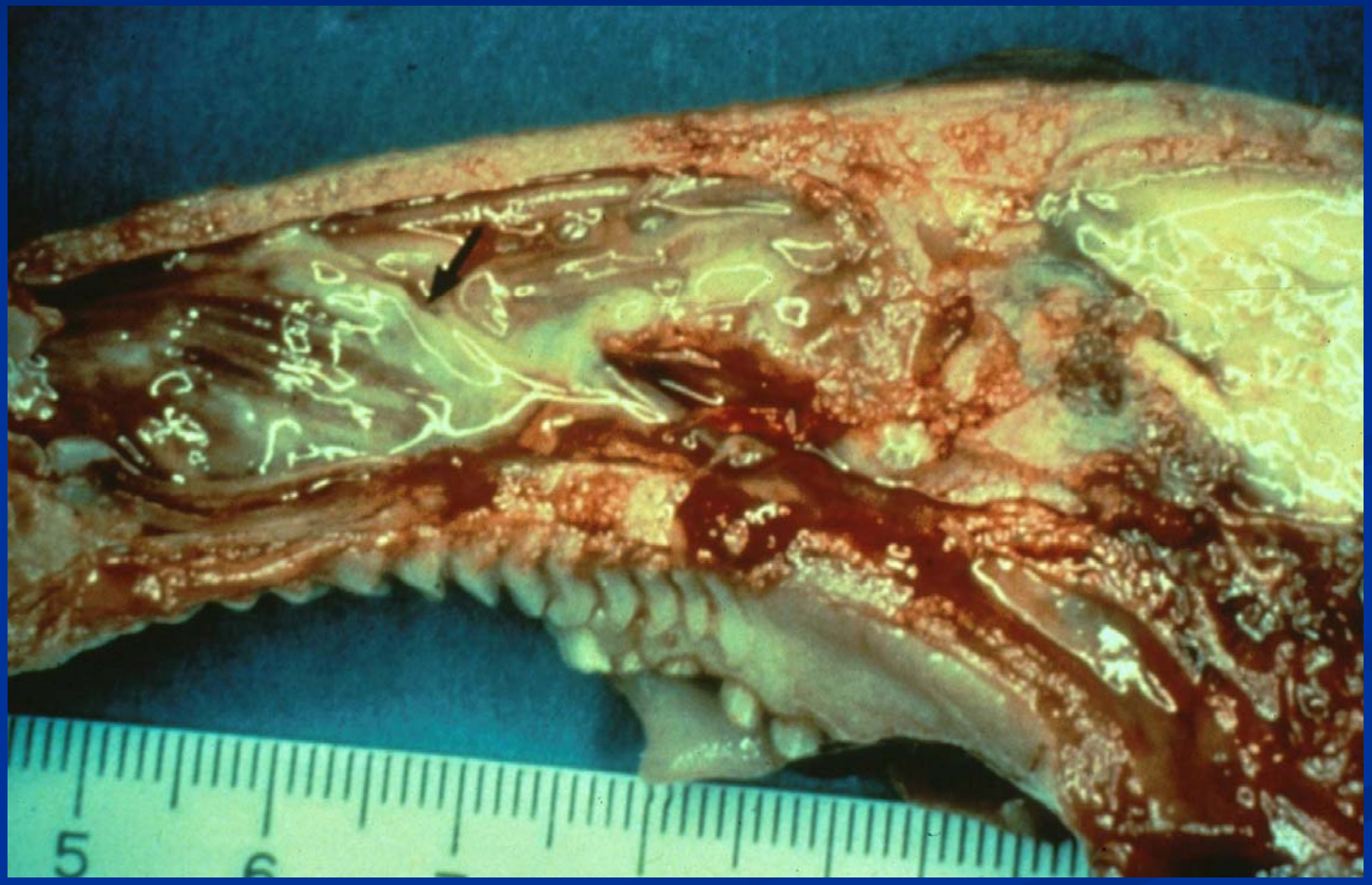
- *Pasteurella multocida*
- *Bordetella bronchiseptica*
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- All cause similar lesions
- CAR associated bacillus – different antigenically from that in mice and rats

Pasteurella multocida

- Major disease in rabbits - incidence up to 50% with up to 70% harboring organism in URT and tympanic bullae.
- Lesions: chronic rhinitis (snuffles) and bronchopneumonia.
- Transmitted by direct contact with nasal or vaginal secretions. Fomites may be involved
- Predisposing factors: ammonia, pregnancy, concomitant disease
- Spread: middle ear via the eustachian tube; hematogenously; local extension; and to the genital tract by venereal spread

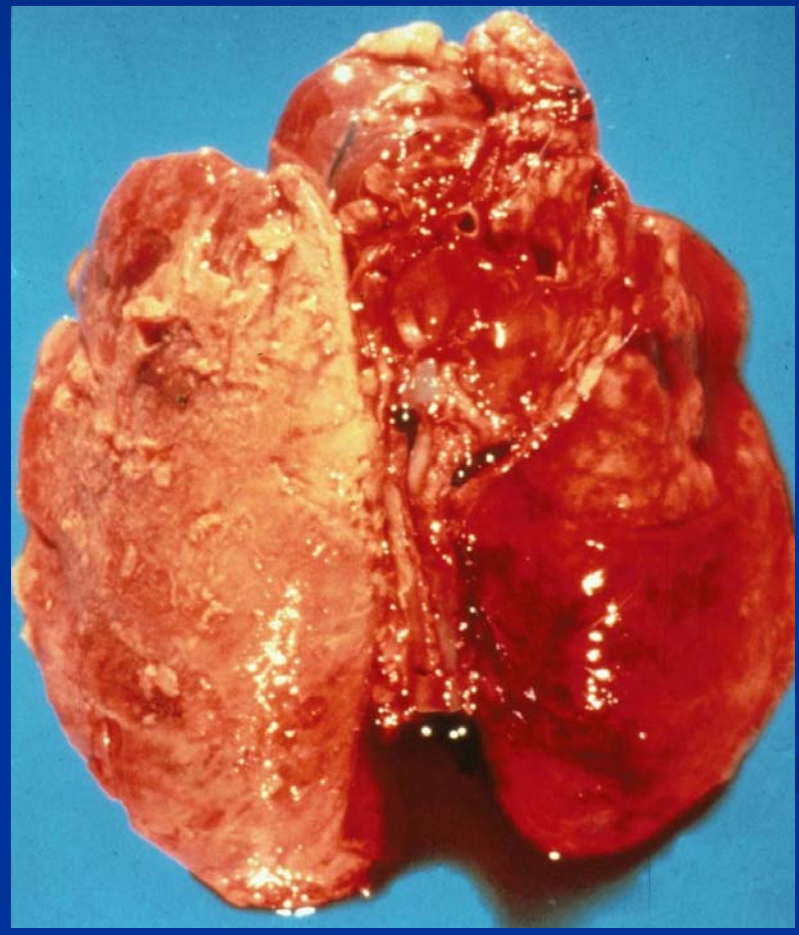
Pasteurella multocida—Rabbit

Suppurative Rhinitis - Snuffles



Pasteurella multocida—Rabbit

- Fibrinous pleuritis
- Bronchopneumonia



Staphylococcus aureus

- Septicemia and purulent bronchopneumonia. Most strains hemolytic, coagulase - +ve, type C
- Tansmitted by direct contact via aerosol. Umbilical vessels and skin abrasions possible entry sites.
- Spreads hematogenously or via local extension.
- Pneumonia often very suppurative with focal necrotizing lesions with colonies of cocci.

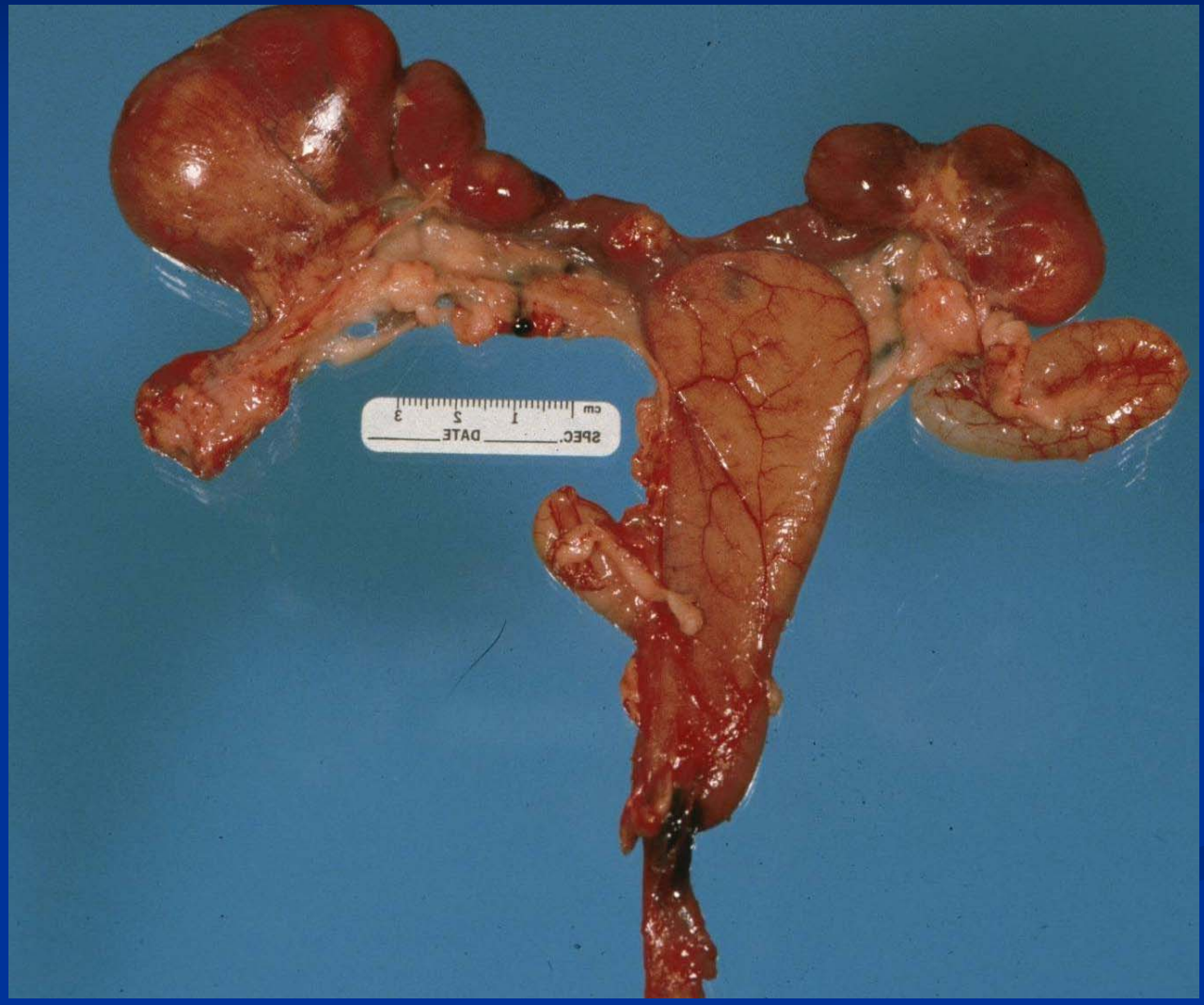
Bordetella bronchiseptica

- Often with *Pasteurella multocida* - role in disease not established.
- Can be recovered from the upper and lower respiratory tract of healthy rabbits.
- Chronic bronchointerstitial pneumonia with perivascular and peribronchial accumulations of lymphocytes, plasma cells, and macrophages.

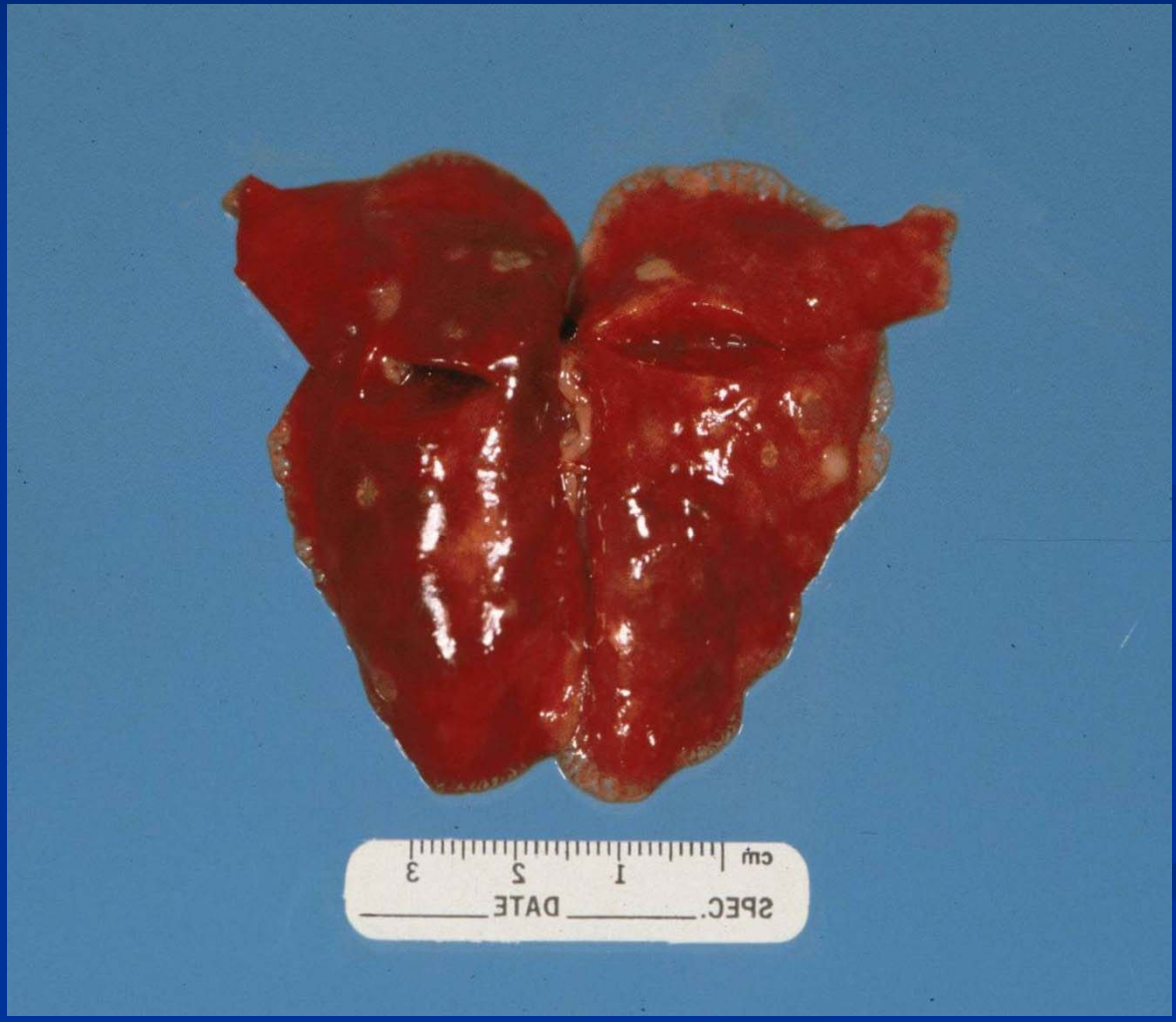
Pulmonary Neoplasia

- Rabbits extremely susceptible to uterine carcinoma which can metastasize to the lungs
- Up to 80% by 5 years of age

Uterine Adenocarcinoma--Rabbit



Pulmonary Metastasis from Uterine Adenocarcinoma



Respiratory Disease of Guinea Pigs

- Anatomic feature - thick medial walls of pulmonary vessels
- Background lesions often include severe inflammation
- Infectious agents: *Bordetella, S. pneumonia, S. zooepidemicus, Klebsiella, Pasteurella multocida, P. aeruginosa, C. freudii, S. aureus,*

Respiratory Disease of Hamsters

- **NonInfectious**
- Congestive heart failure
- **Viruses – as mice and rats**
- Sendai virus
- MPV (murine pneumonia virus)
- **Bacteria**
- *Pasteurella pneumotropica*
- *Streptococcus pneumonia*
- *Streptococcus agalactiae*
- *Mycoplasma pulmonis*

Respiratory Disease of Ferrets

- Non infectious lesions
  - Aspiration pneumonia
  - Endogenous lipid pneumonia
- Infectious diseases
  - Canine distemper
  - Influenza - human

Respiratory Pathology of Non Human Primates

- Viruses
  - Cytomegalovirus
  - Other herpes viruses - lung involvment as part of systemic disease -focal necrosis with/without intranuclear inclusion bodies
  - Measles
  - Adenovirus
- Bacteria
- Fungi
- Parasites

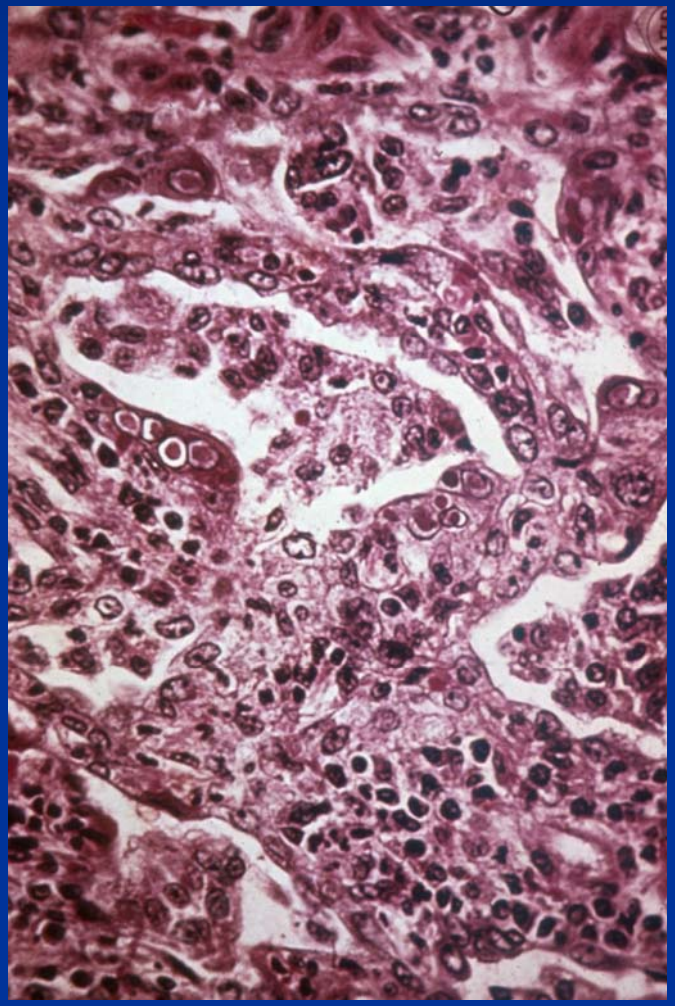
Cytomegalovirus

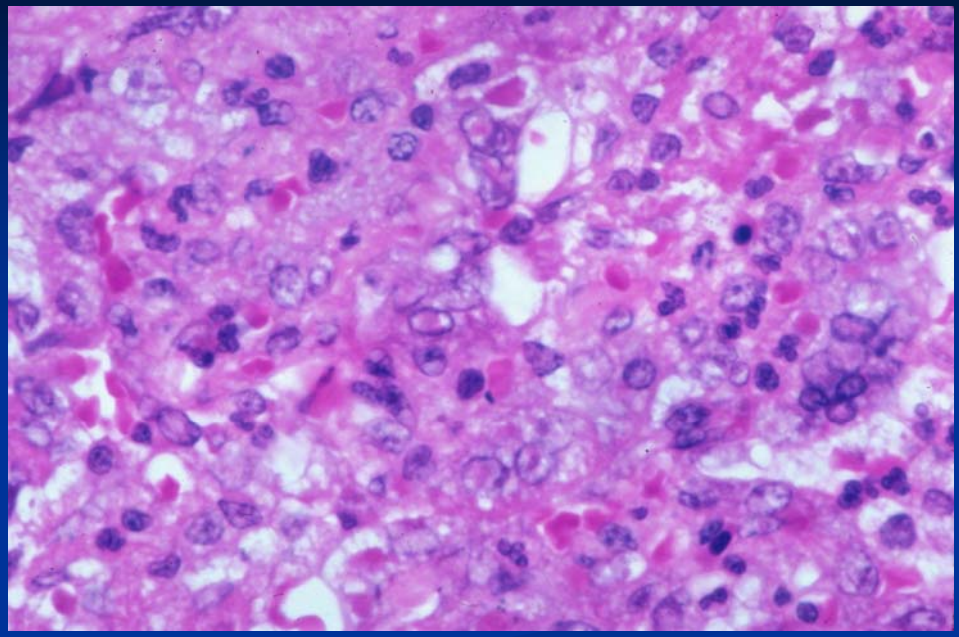
- *Etiology:* Betaherpesvirus
- Highly species-specific
- *Transmission:* shed in urine, may be acquired transplacentally
- *Clinical:* Usually none. Disease only in fetuses and immunodeficient. CNS and respiratory t signs may be noted
  - In macaques, widespread latent infection with most seroconverting during the first year of life.
  - Common opportunistic infection in SIV- and SRV-infected macaques.

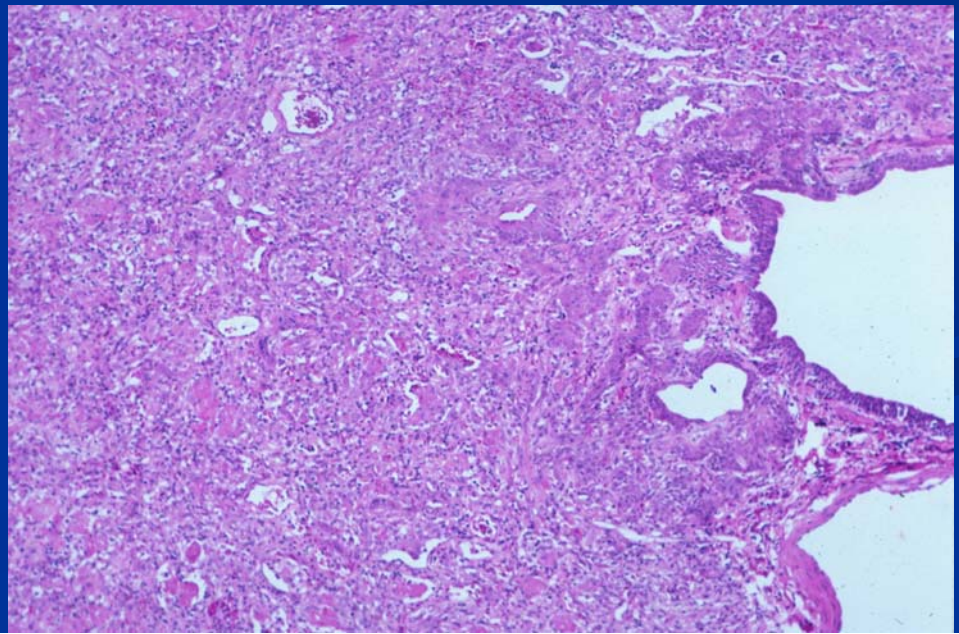
Pathology: Cytomegalovirus Infection

- In immunodeficient animals, generalized infection - necrotizing meningitis and neuritis, interstitial pneumonia, arteritis, enterocolitis, orchitis, and focal necrosis in liver and spleen.
- Infects mesenchymal cells, rather than epithelium
- Cells often enlarged, may contain large basophilic INIB and granular eosinophilic ICIB.

Measles - Monkey



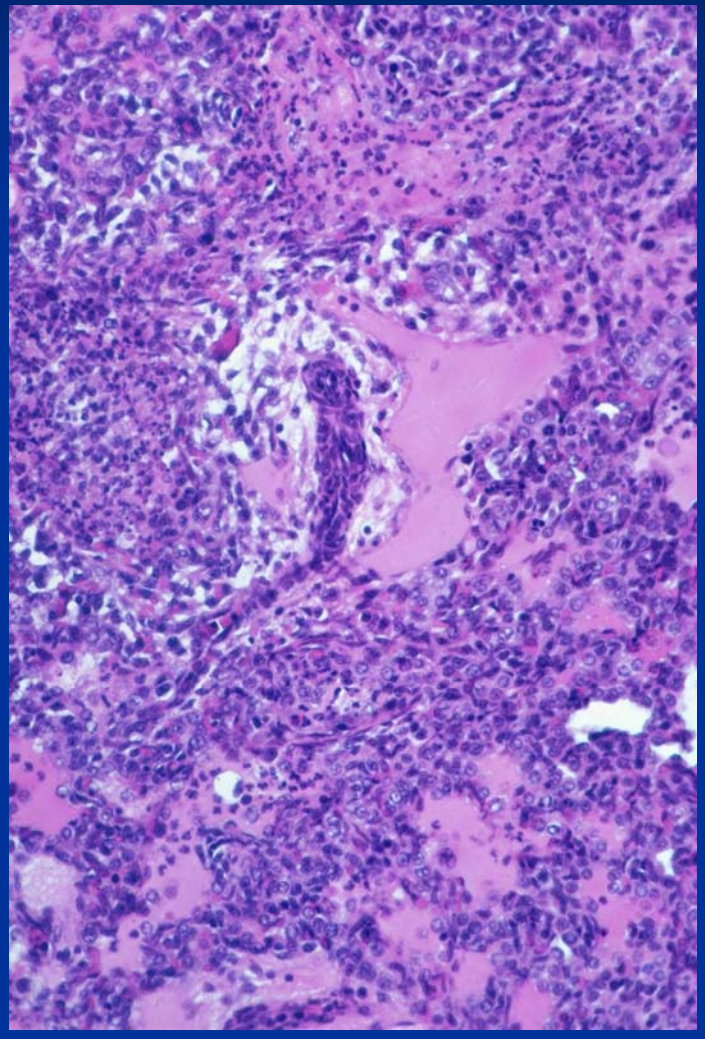


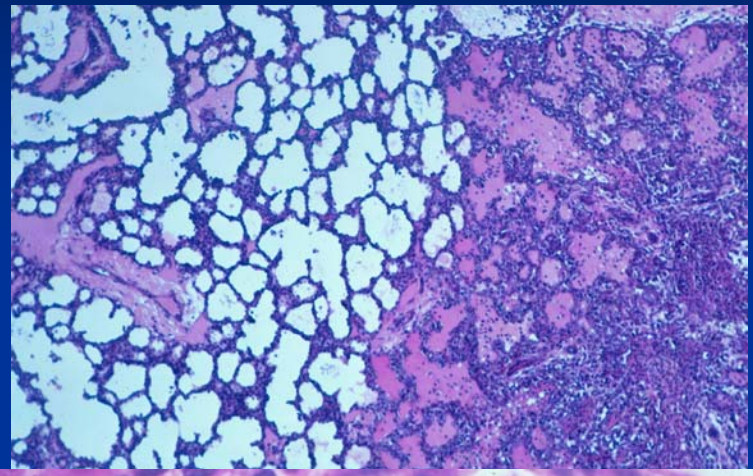


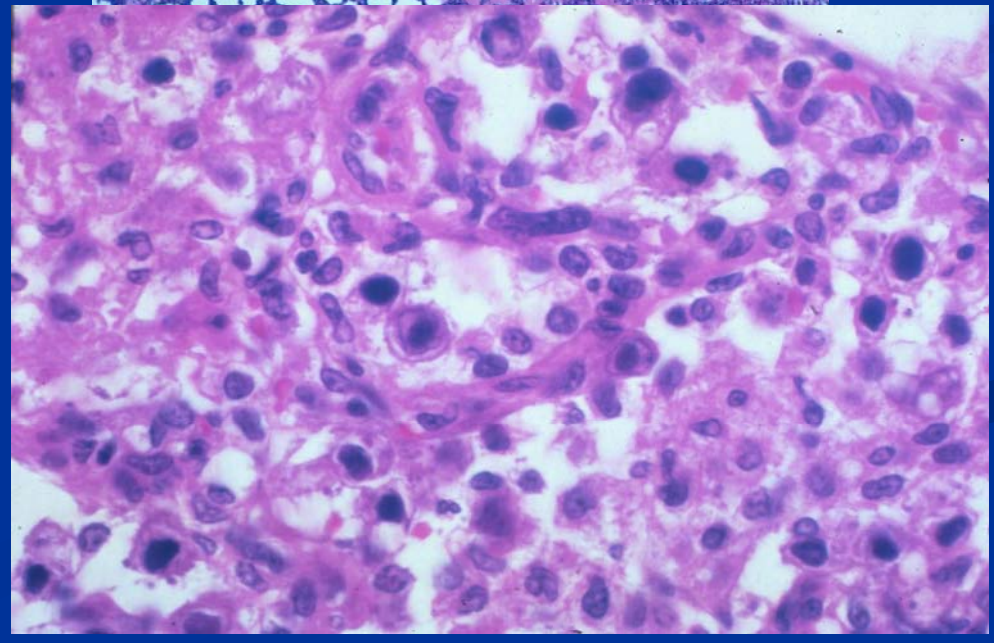
Adenovirus

- *Etiology*: Adenovirus
- *Clinical:* Usually no clinical signs, but virus can be isolated. In some cases, conjunctivitis and respiratory infections, diarrhea, and pancreatitis in rhesus. Severe infections in immunodeficient animals.
- *Pathology:* In immunodeficient monkeys, necrotizing bronchointerstitial pneumonia, pancreatitis and enteritis
    - Intranuclear inclusions vary in size and color

Adenovirus—Fetal Monkey







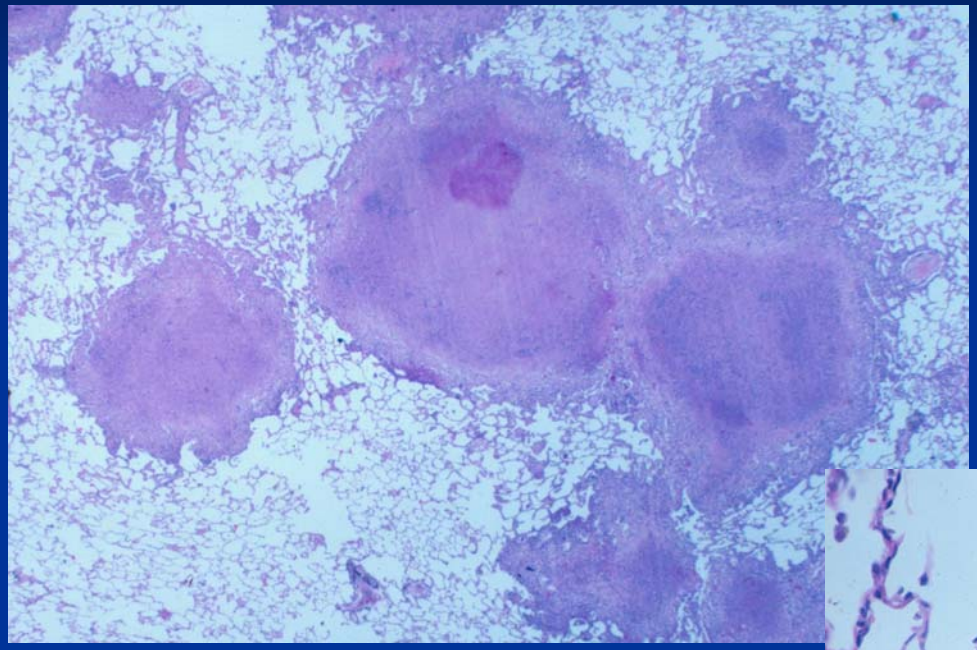
Respiratory Pathology of Non Human Primates

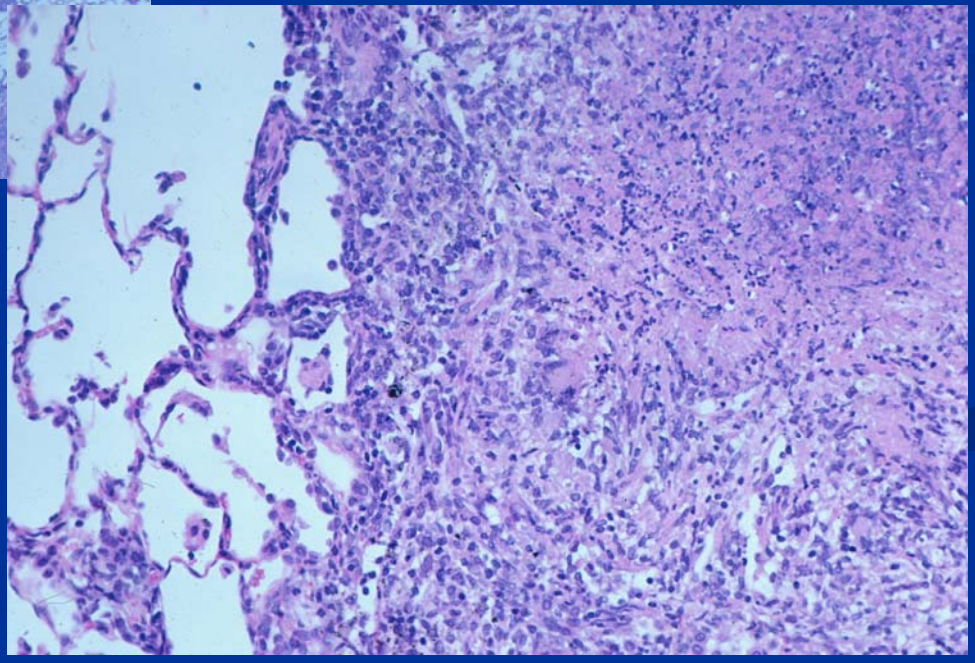
- Viruses
- Bacteria
  - *Mycobacterium spp*
  - *Streptococcus pneumoniae*
  - *Bordetella bronchiseptica*
  - *Klebsiella pneumoniae*
  - *Nocardia sp*
- Fungi
- Parasites

Tuberculosis

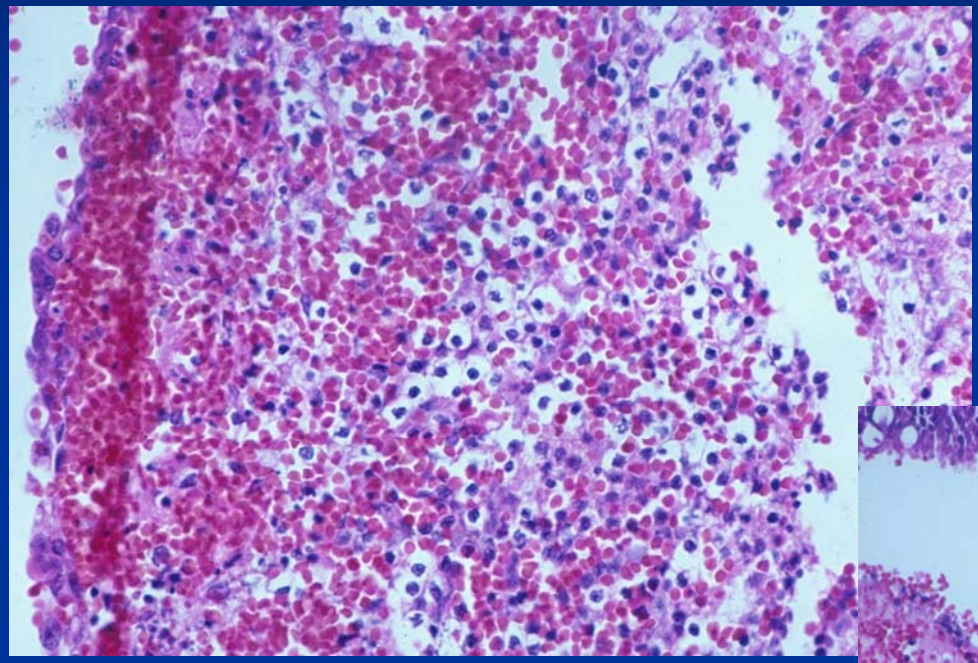
- *Etiology*: *Mycobacterium tuberculosis, M. bovis*, atypical mycobacteria
- *Transmission:* Respiratory, oral. *M. tuberculosis* and *M. bovis* typically acquired from humans or ruminants in country of origin. Tuberculosis is rare in wild populations.
- *Clinical:* Rapidly progressive disease. Often no clinical signs. New World monkeys more resistant than OWM
  - Severely affected - coughing, wasting, enlarged lymph nodes, splenomegaly, and hepatomegaly
  - Most cases diagnosed by tuberculin testing in quarantine

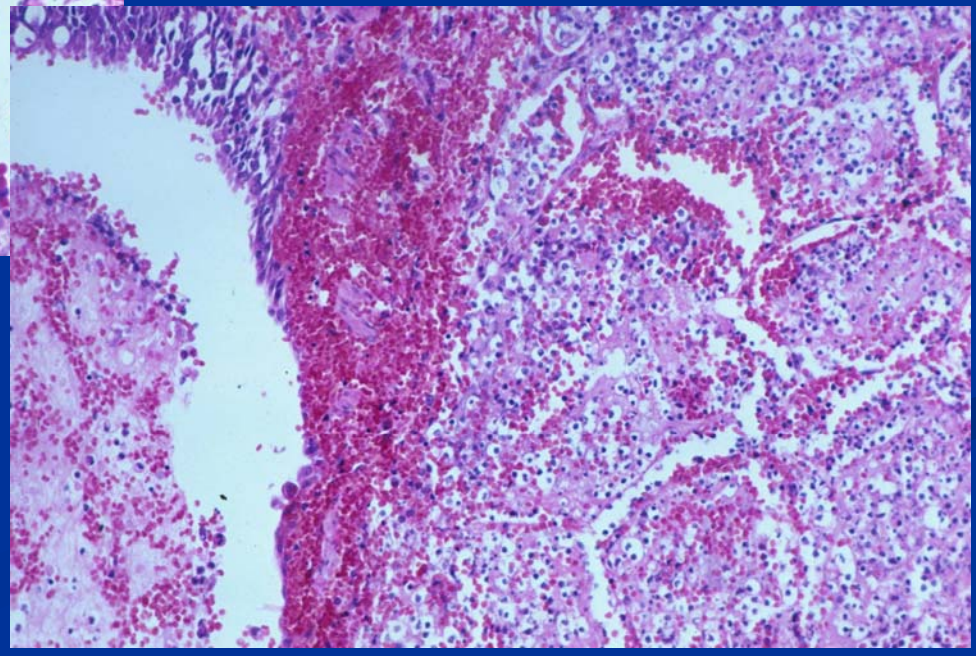
Tuberculosis—Primate





Streptococcus pneumoniae— Monkey





Bordetellosis

- Etiology: *Bordetella bronchiseptica*
- Transmission: aerosol
- Clinical: often asymptomatic. Mucopurulent nasal discharge, dyspnea, and death reported.
- Pathology: Fibrinopurulent hemorrhagic bronchopneumonia
- References:
  - Graves IL. Lab Anim Care 18:405-406, 1968.
  - Kohn DF, et al. Lab Anim Sci 27:279-280, 1977.
  - Seibold HR, et al.. Lab Anim Care 20:456-461, 1970.

Klebsiella sp.

- *Etiology: Klebsiella pneumoniae*
- *Transmission:* respiratory, carried in nose and throat
- *Clinical:* nasal discharge, pneumonia, meningitis, or serositis.
- *Pathology:* Fibrinopurulent pneumonia, serositis, and septicemia.
  - Macrophages often predominate in pulmonary lesions
  - Abundant Gram neg bacteria with prominent capsules in exudates which may be gelatinous

Nocardiosis

- *Etiology: Nocardia asteroides*
- *Transmission:* inhalation and ingestion - organisms in soil and organic material
- *Clinical:* often associated with defects in cellular immunity.
- *Pathology:* infections predominant in lungs, but may disseminate.
- Mixed inflammatory infiltrates, abscesses, and granulomas are found.
- G-positive, filamentous, branching, often beaded, and variably acid-fast.

Respiratory Pathology of Non Human Primates

- Fungi
  - *Pneumocystis carinii*
- Parasites
  - *Toxoplasma gondii*
  - Mites
  - Lungworms
  - Other

Pneumocystosis

- *Etiology: Pneumocystis carinii*
- *Transmission:* aerosol, may be horizontally acquired or reactivated latent infections
- *Clinical:* only in immunodeficient animals - fever, dyspnea, and cough
- *Pathology:* foamy eosinophilic intra-alveolar exudate mixed with alveolar macrophages, interstitial lymphocytic infiltration, and type II cell hypertrophy.

Toxoplasmosis

- *Etiology: Toxoplasma gondii*
- *Transmission:* ingestion of food contaminated by cat feces or ingestion of raw meat. NHP will catch and eat rodents that may be infected. Primates in the wild are rarely seropositive. Epizootics have occurred in captive New World species.
- *Clinical:* NWM more susceptible than OWM, which are usually asymptomatic. Lethargy, CNS signs, and sudden death may occur.

Toxoplasmosis

- *Pathology:*
  - Pulmonary edema, lymphadenopathy, splenomegaly, and intestinal ulceration
  - Necrosis, with or without inflammation, in liver, spleen, lymph nodes, heart, lung, adrenal, intestinal muscle, and brain
  - Individual organisms and cysts found

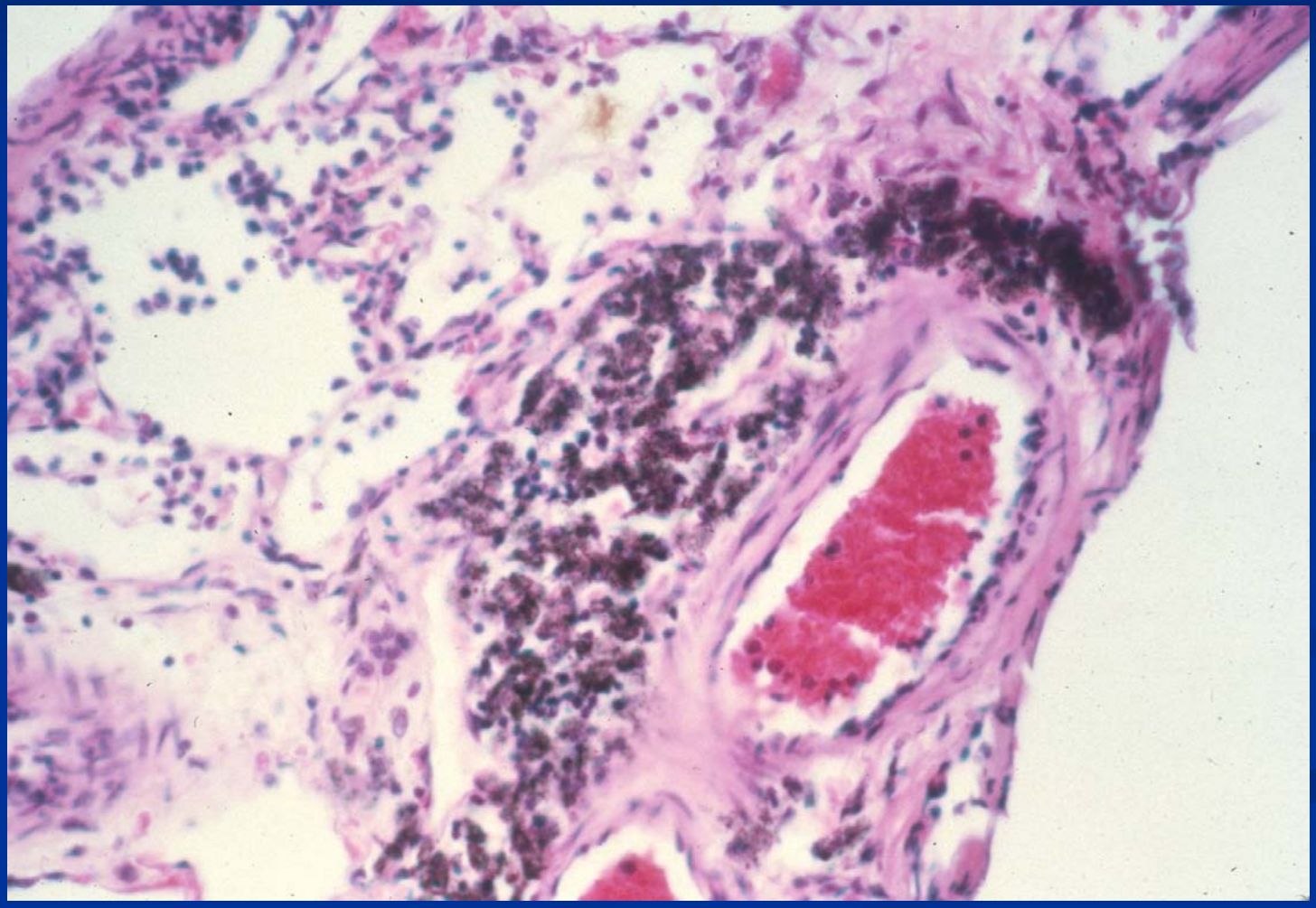
Respiratory Mites

- *Etiology: Pneumonyssus* and *Pneumonyssoides* spp. in lungs, *Rhinophaga* in nasal cavity.
- *Pneumonyssus simicola* - nearly 100% incidence in rhesus monkeys until advent of ivermectin
- *Transmission:* Unknown, but close contact required.
- *Clinical*: usually no clinical signs. Rarely pneumothorax due to rupture of a "mite house." Lung mites can cause serious clinical disease in langurs and proboscis monkeys.

Respiratory Mites

- *Gross pathology*: Focal, yellow, air-filled cysts 1-10 mm in diameter, raised if on pleural surface.
- *Histopathology:* chronic bronchiolitis with bronchiectasis and eosinophilic granulomatous inflammation, cross sections of mites, and golden brown refractile pigment.
- Bronchial lymph nodes pigmented due to mite pigment.

Mite Pigment—Primate



Lungworms

- *Etiology: Filaroides sp* and *Filariopsis sp*
- *Transmission:* larvae in feces, rest unknown
- *Clinical:* most common in NWM, no clinical signs
- *Pathology:* 1-2-mm focal brown irregular pleural foci,
  - small slender adults in terminal bronchioles and alveoli
  - females are viviparous

Strongyloides

- *Etiology: Strongyloides cebus* in NWM, *S. fulleborni* in OWM.
- *Transmission:* orally and by skin penetration
- *Clinical:* usually asymptomatic, but diarrhea can result. Coughing may be associated with larval migration
- *Lung pathology:* hemorrhage of due to migrating larvae.

Anatrichosoma

- *Etiology: Anatrichosoma cutaneum, A. cynomolgi*
- *Transmission:* embryonated eggs deposited in nasal or cutaneous epithelium and sloughed.
- *Clinical:* mild peeling of epidermis of palms and soles. May see serpentine tracks with intense inflammation.
- *Pathology:* Worms and eggs in cross sections of nasal epithelium or skin of face, hands and feet with little inflammation.
- *Comment*: seldom see when routinely treated with anthelminthics.

Pathology of Laboratory Animals

- Acknowledgements
  - http://www.afip.org/vetpath/POLA2005.pdf
    - Mouse and Rat – Steve Barthold
    - Rabbit – Lyn Raymond
    - Primates – Gary Baskin
  - http://www.radil.missouri.edu/info/dora/mousepag/resp.html
- Resources
  - Diagnostic Pathology
    - Percy DH and SW Barthold, 2nd Edn (2001) "Pathology of Laboratory Rodents and Rabbits" Iowa State University Press.
  - Jackson labs website: jaxmice.jax.org

Resources

- *The Handbook of Experimental Animals: The Laboratory Mouse,* Hedrich, HJ, Bullock, G, Petrusz, P, Eds. 2004. Elsevier Academic Press, San Diego, California. pp.225-243.
- *Pathology of the Mouse,* GA Boorman Ed, 1999. Cache River Press, pp.293 332.
- Hardin JD. *Genetically engineered mice as models for human disease*. P&S Medical Review. 1994.
- Sundberg, JP and Boggess D. Systematic Approach to Evaluation of Mouse Mutations, 2000. CRC Press LLC.
- Ward, JM, Mahler, JF, Maronpot, RM, and Sundberg, JP. *Pathology of genetically engineered mice*. 2000. Iowa State University Press, Ames, Iowa. pp. 161-179.

Resources

- AALAC publications e.g. Bennett, BT et al, (1998) "Non Human Primates in Biomedical Research, Diseases" Academic Press. Coming – Biology of the Laboratory Mouse
- Haschek W.M., H. P. Witschi, and K. Nikula. Respiratory system. In: *Handbook of Toxicologic Pathology*. Haschek, W. M., Rousseaux, C.G., and Wallig, M.A. 2nd Ed., 2002. Academic Press, San Diego, California. pp. 3-83