

January 2007

Whats Your Diagnosis ?

Tissue from a
mouse.

H&E.



January 2007

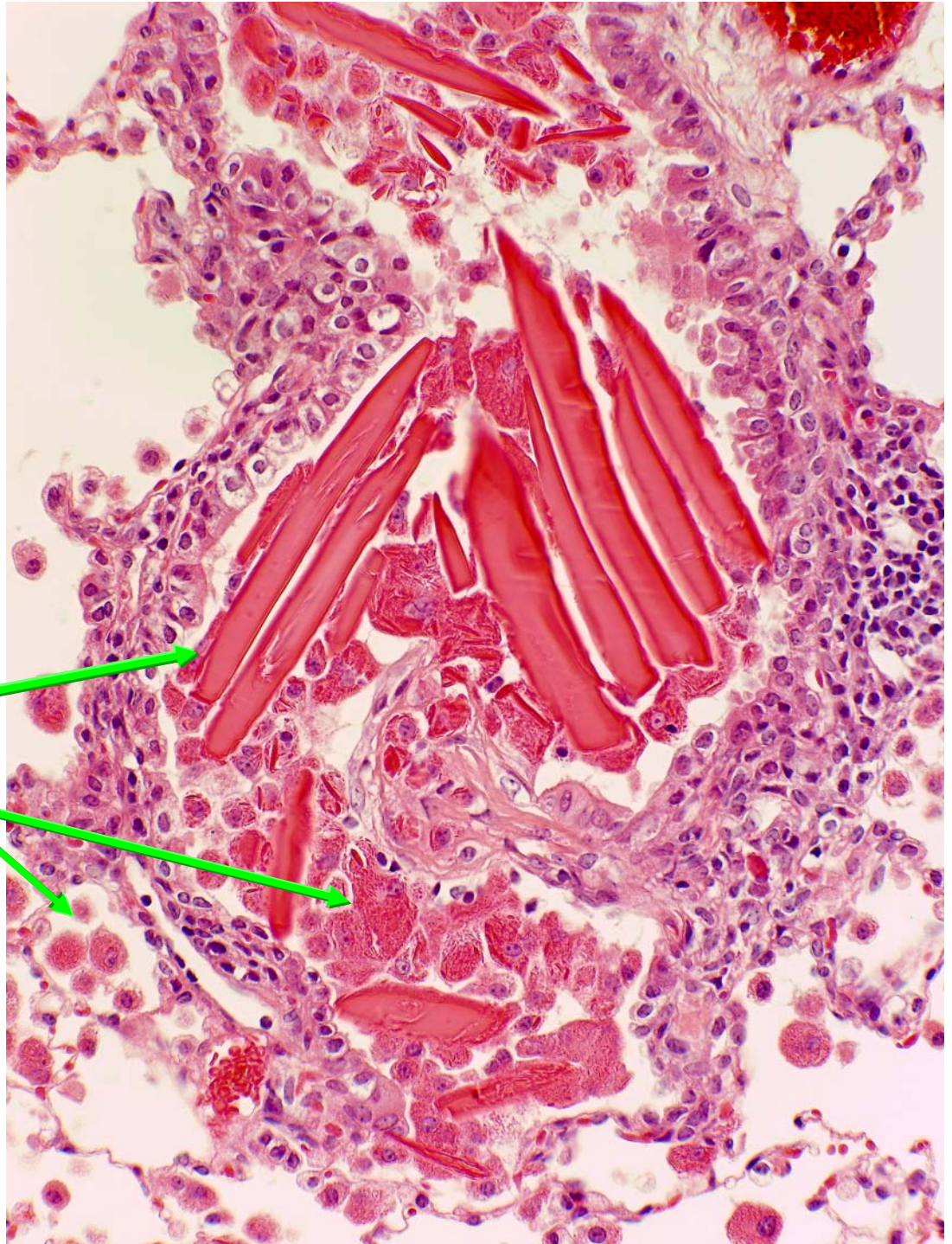
Whats Your Diagnosis ?

Diagnosis:

Lung. Acidophilic crystalline pneumonia, aka acidophilic (eosinophilic) macrophage pneumonia.

Lung. Bronchiole contains prominent acidophilic/eosinophilic, extracellular crystals, up to 100 u long. Bronchiole and alveoli contain abundant plump macrophages up to 50u diam, distended by smaller intracytoplasmic acidophilic/eosinophilic crystals.

Comments below.



January 2007

Whats Your Diagnosis ?

Comments. The condition is not uncommon in a wide variety of mice, including C57BL/6, 129, Swiss and related strains and stocks. It has been recognized in mice since the early 20th century. In some cases (like this) the extracellular crystals are striking. In other cases (Fig 2) the histiocytic component is profound. Severity of the condition and degree of pulmonary involvement varies from subtle changes to severe and diffuse involvement that should be expected to have contributed to the clinical deterioration or demise of the host, and should be expected to impact a variety of phenotypes and studies. Recently the material has been identified as a chitinase (YM1 and or YM2), which may be produced by macrophages, neutrophils or epithelial cells. The material and or crystals also have been identified in nose, stomach, gall bladder, bone marrow and other tissues, where the condition has been termed hyalinosi.

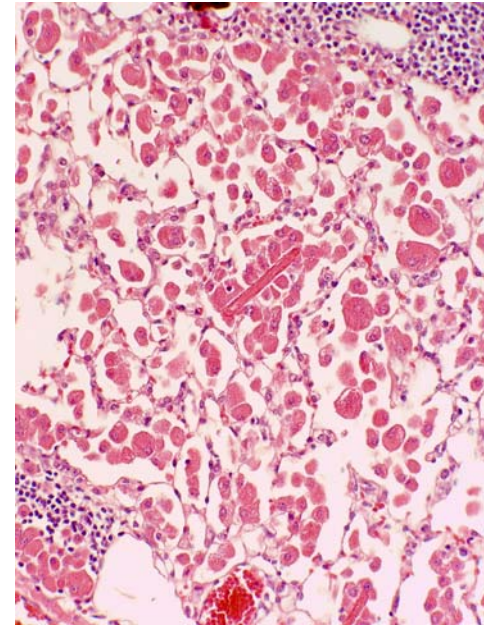


Fig 2



Mouse Acidophilic Macrophage Pneumonia and Hyalinosis - Suggested References

Elizabeth Ufford-Green. 1942. On the occurrence of crystalline material in the lungs of normal and cancerous Swiss mice. (Bryn Mawr PhD thesis, Clara Lynch's Swiss mice)

- *Large extracellular crystal plates are found frequently in the lumina of bronchioles. Less commonly they are lodged within the walls of alveoli. In each case they are accompanied by masses of dust cells...*
- Similar structures noted previously by Haaland (1905) & Tyzzer (1909).

Ward JM. 1978. Pulmonary pathology of the moth-eaten mouse. *Vet Pathol* 15(2):170-8

- unusual pneumonia = cause of natural death of mice by 7 weeks of age.
- focal accumulations of alveolar macrophages in alveoli, especially adjacent to bronchioles.
- Needle-like crystals in lysosomes of macrophages
- Numerous crystal laden macrophages filling most alveoli in 5-7-week-old mice.
- The unusual pneumonia was the only lesion severe enough to cause death.

Murray & Luz. 1990. Acidophilic macrophage pneumonia in laboratory mice. *Vet Pathol* 27(4):274-81.

- Characterized by accumulations of crystalloid-laden alveolar macrophages, was seen in 30/7,500 NMRI, 7/600 T x HT, 2/100 C57BL and in *no cases of 1,500 CBA and 1,100 BALB/c mice.*
- large numbers of eosinophilic macrophages, were generally associated with granulocytes.
- Macrophages could be mononucleate or multinucleate and had a crystalline cytoplasm.
- Free-lying crystals were sometimes observed.

Continued...



Mouse Acidophilic Macrophage Pneumonia and Hyalinosis - Suggested References

Haines et al. 2001. Toxicol Pathol. 29(6):653-61. Pathology of aging B6;129 mice.

- Hyalinosis with extracellular crystals in several tissues (respiratory tract, gall bladder, stomach)

Ward et al. 2001. Hyalinosis and Ym1/Ym2 gene expression in the stomach and respiratory tract of 129S4/SvJae and wild-type and CYP1A2-null B6, 129 mice. Am J Pathol. 158(1):323-32.

- Hyalinosis (eosinophilic cytoplasmic change) in glandular stomach, respiratory tract, bile duct, and gall bladder of B6,129 CYP1A2-null & wild-type mice + both sexes of background 129S4/SvJae strain.
- Ym1 in normal and abnormal nasal olfactory + respiratory epithelium, pulmonary alveolar macrophages, bone marrow myeloid cells, squamous forestomach epithelium + glandular stomach epithelium.
- Ym2 identified from hyaline gastric lesions

Nio et al. 2004. Histochem Cell Biol.121(6):473-82. Cellular expression of murine Ym1 and Ym2, chitinase family proteins, as revealed by in situ hybridization and immunohistochemistry.

- Chitinase family proteins, widely distributed, bind GAG's such as heparin/heparan sulfate.
- Ym1 is a macrophage protein produced in parasitic infections...
 - Lung -- Ym1-expressing cells are alveolar macrophages, Ym1 localized in RER.
 - Spleen --Ym1-expressing cells in the red pulp identified as immature neutrophils.
 - Marrow -- immature neutrophils immunoreactive → lose immunoreactivity with maturation.
 - Marrow -- needle-shaped crystals in macrophages showed intense Ym1 immunoreactivity.
- Ym2 expression restricted to gastric squamous epithelium in junctional region

