

# **Granulomatous lung diseases**

**An approach to the differential  
diagnosis**

## **Reference**

Arch Pathol Lab Med 2010;134:667-690.

Granulomas are among the most commonly encountered abnormalities in pulmonary pathology. Granuloma is a compact aggregate of histiocytes (macrophages) which are described as epithelioid cells.

Aggregate of histiocytes is a minimum requirement of a granuloma regardless of whether the lesion also contains necrosis, lymphocytes, plasma cells or multinucleated giant cells.

# Recommended step-by-step approach to pulmonary granuloma

- 1) Attempt to identify an organism.
- 2) Look for histologic features of noninfectious granulomatous disease.
- 3) If step 1 and 2 do not reveal a specific diagnosis, ensure that an adequate number of blocks have been stained with special stains and re-examine the special stains. If no organisms are found despite thorough reexamination, issue a descriptive diagnosis (necrotizing or non necrotizing).

# Step 1: Identifying organisms

The organisms commonly found in pulmonary granuloma are

**Mycobacteria**

**Fungi**

Histoplasma

Cryptococcus

Coccidioides

Blastomyces

Pneumocystis

Aspergillus

# *Using the tissue reaction as a clue*

**Necrotizing granuloma** in mycobacteria, histoplasma and coccidioides.

**Neutrophils** in granuloma should suggest blastomyces.

**Eosinophils** in granuloma indicates coccidioides.

# *Examining special stains for organisms*

The search for organisms must always begin with hematoxylin- eosin stained sections. Many pathologists incorrectly assume that organisms are not visible on H&E and skip directly to special stains.

The histochemical stains mostly used for identification of organisms are **Ziehl-Neelson (ZN) stain (acid fast stain) for mycobacteria and silver stain for fungi.**

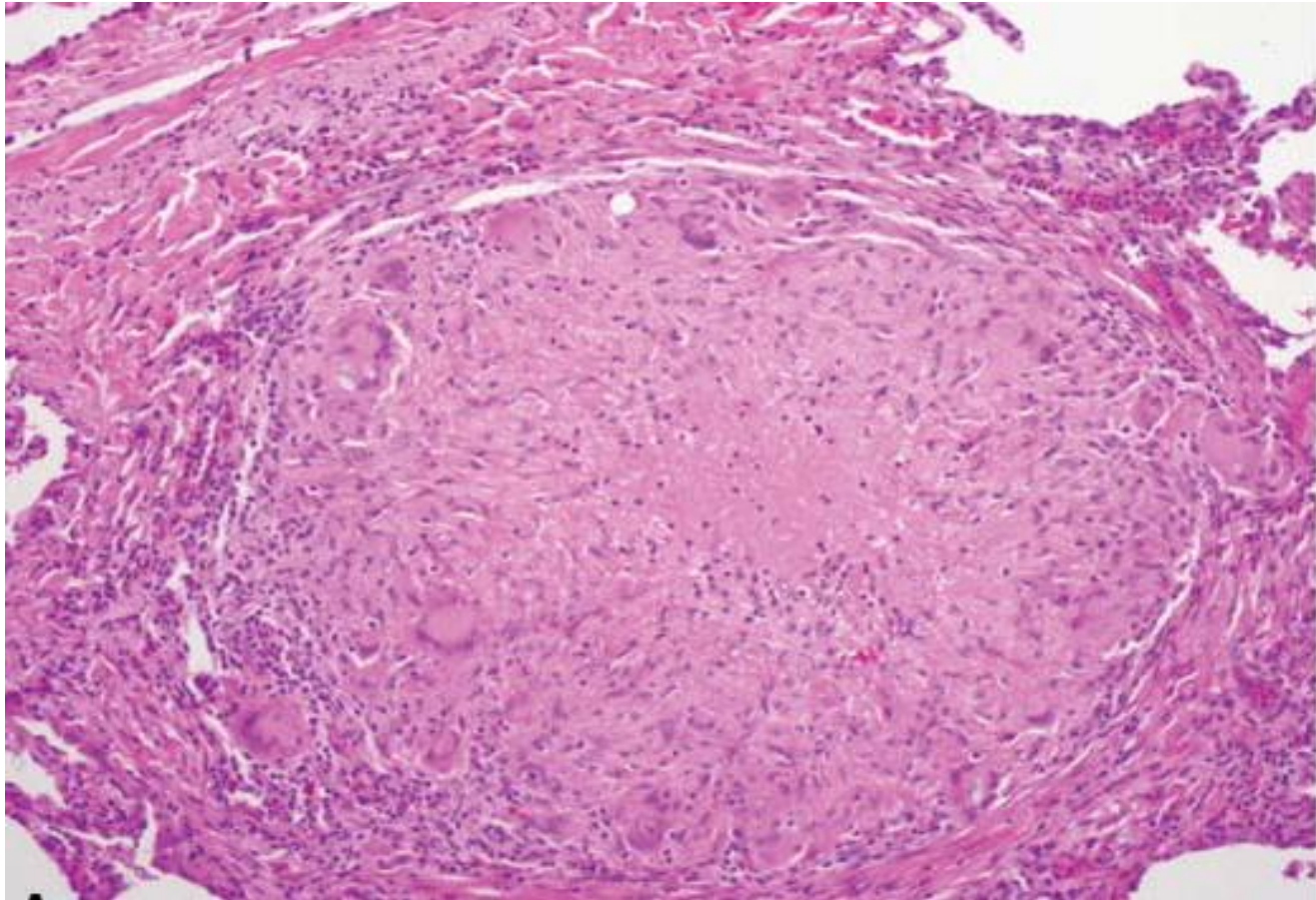
Fluorescence techniques have been shown to be equivalent to culture and superior to acid fast stain.



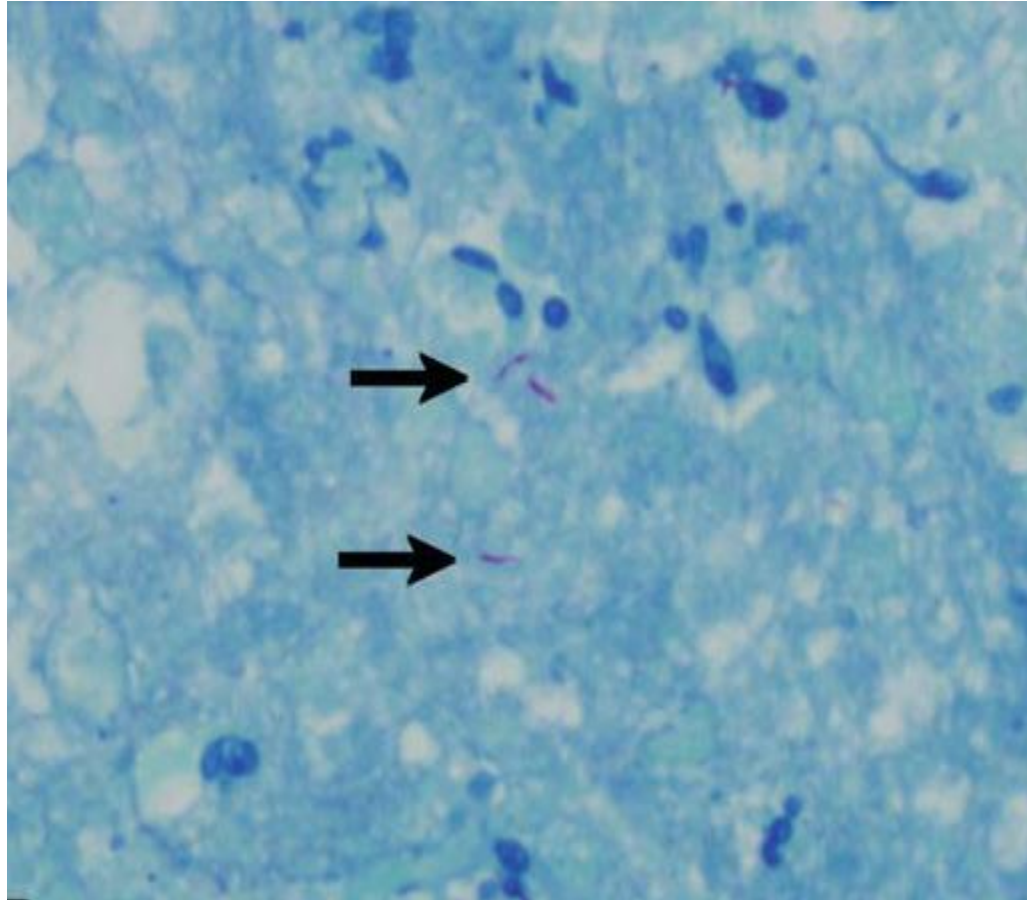
When H&E stained sections are examined, it is recommended to examine silver stained sections before the time consuming ZN stained sections.

The most important point to remember in most cases that mycobacteria are few and difficult to find because of use of xylene in routine processing, and organisms are by far more common in the center of necrosis than at the periphery.

# Necrotizing granuloma of T.B(H&E)



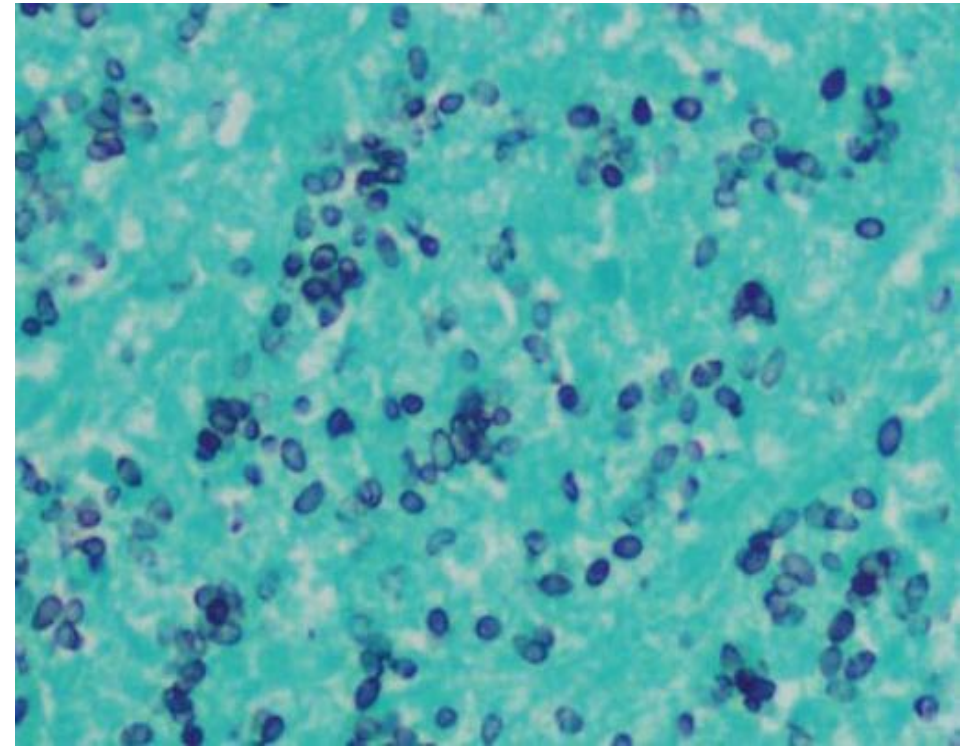
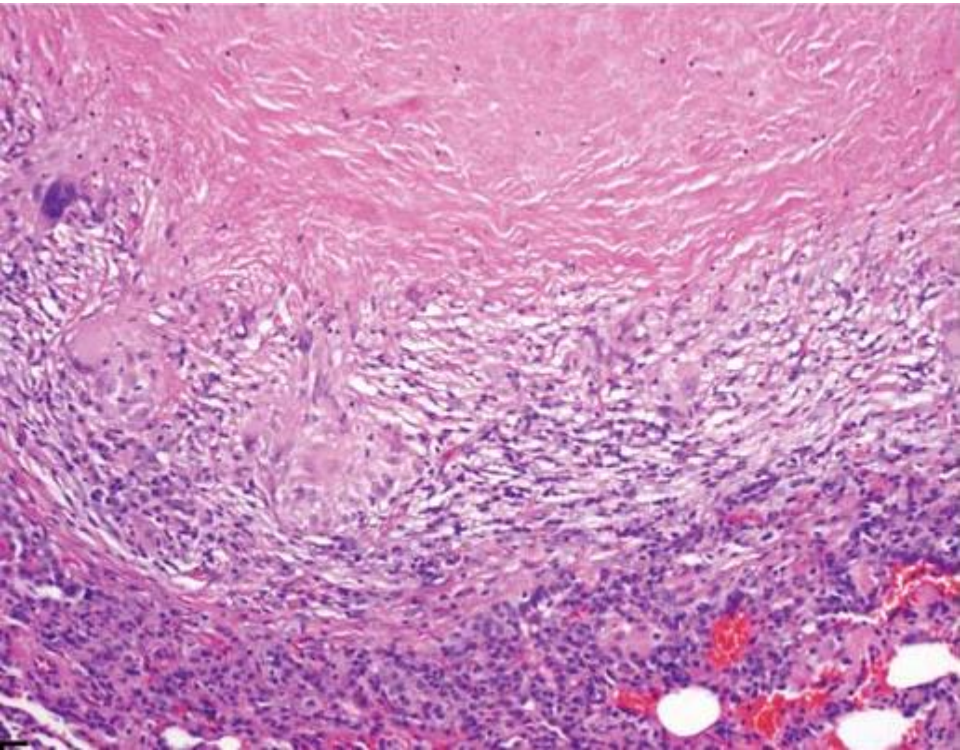
Mycobacteria are demonstrated using  
ZN stained sections



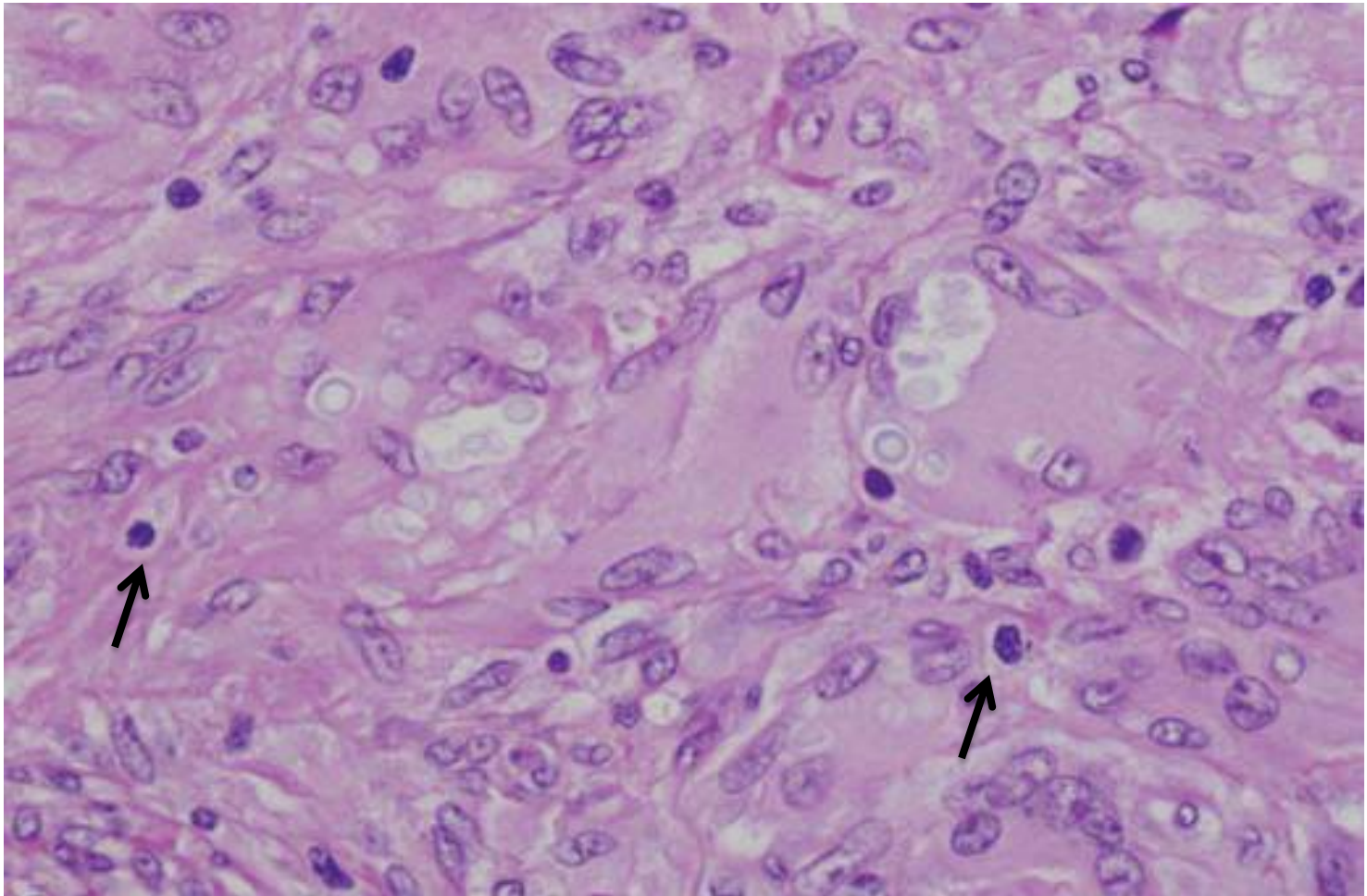


Necrotizing granuloma of histoplasma infection identical to that of T.B

Histoplasma is a small non budding yeast identified using silver stain.

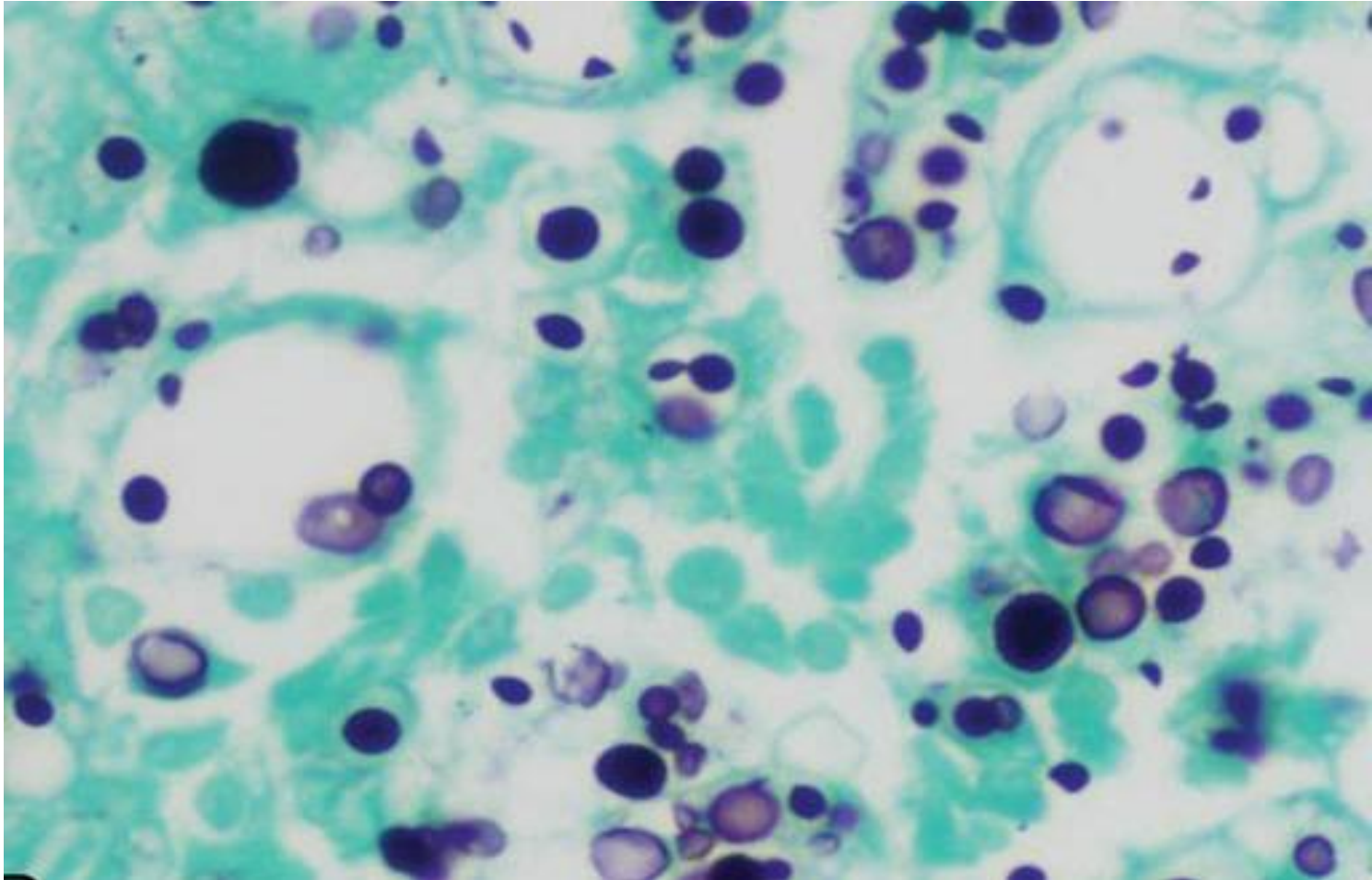


Non necrotizing granuloma of cryptococcus infection, note the round small yeast within histiocyte with halo

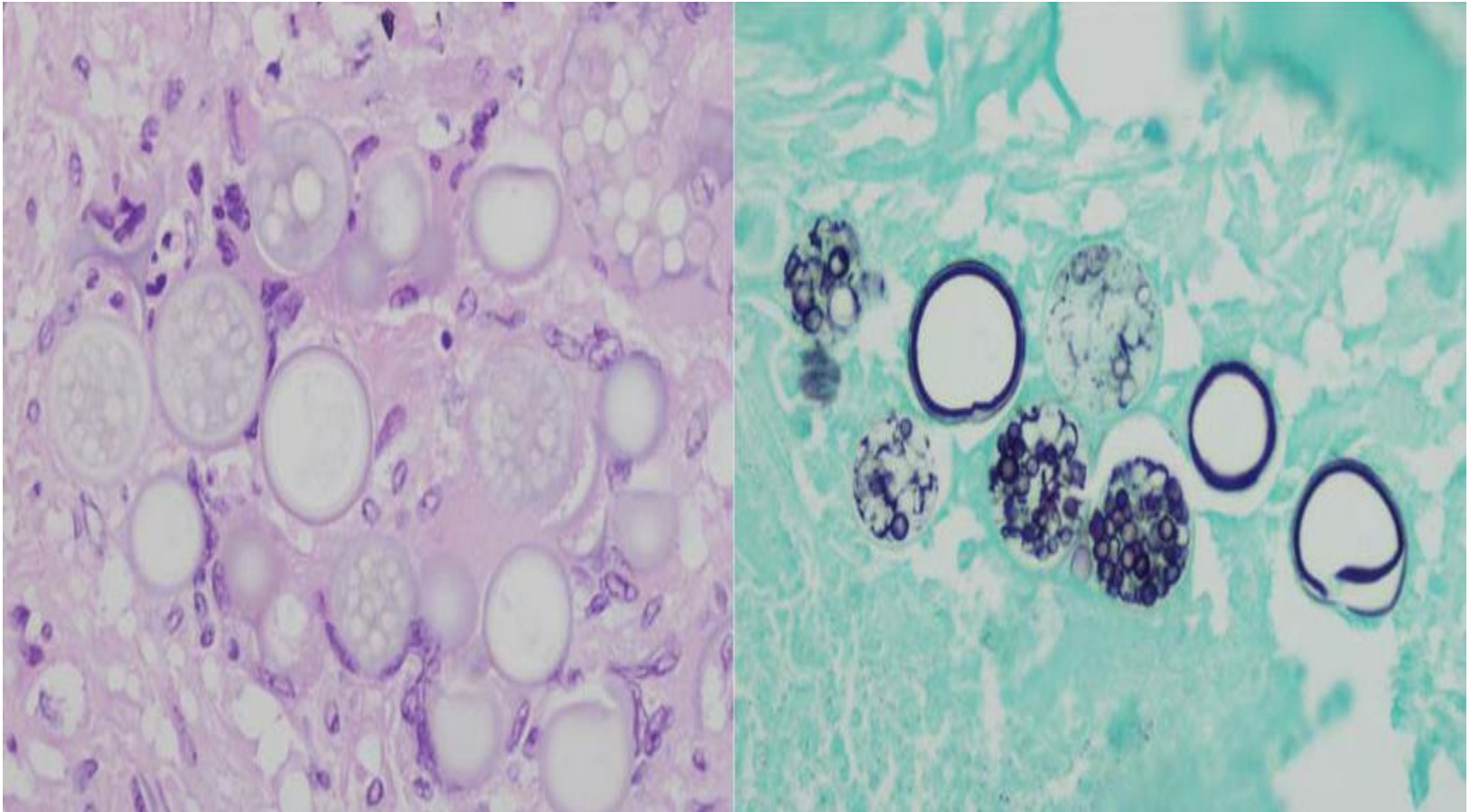




Cryptococcus is a small rounded shaped yeast with marked variation in size demonstrated with silver stain

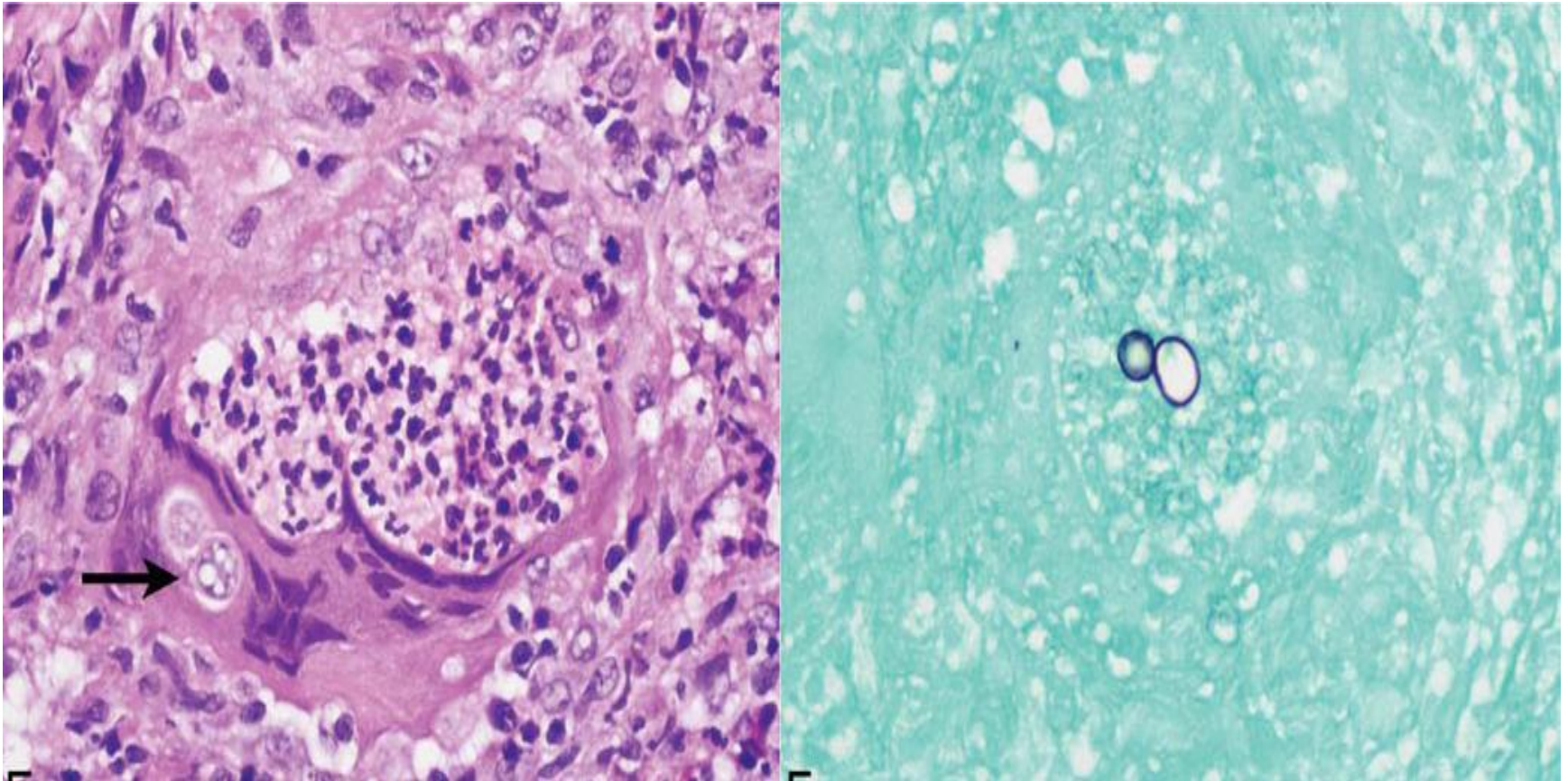


Granuloma of coccidioides: spherules filled with endospore are detected in pulmonary granuloma using both H&E and silver stains



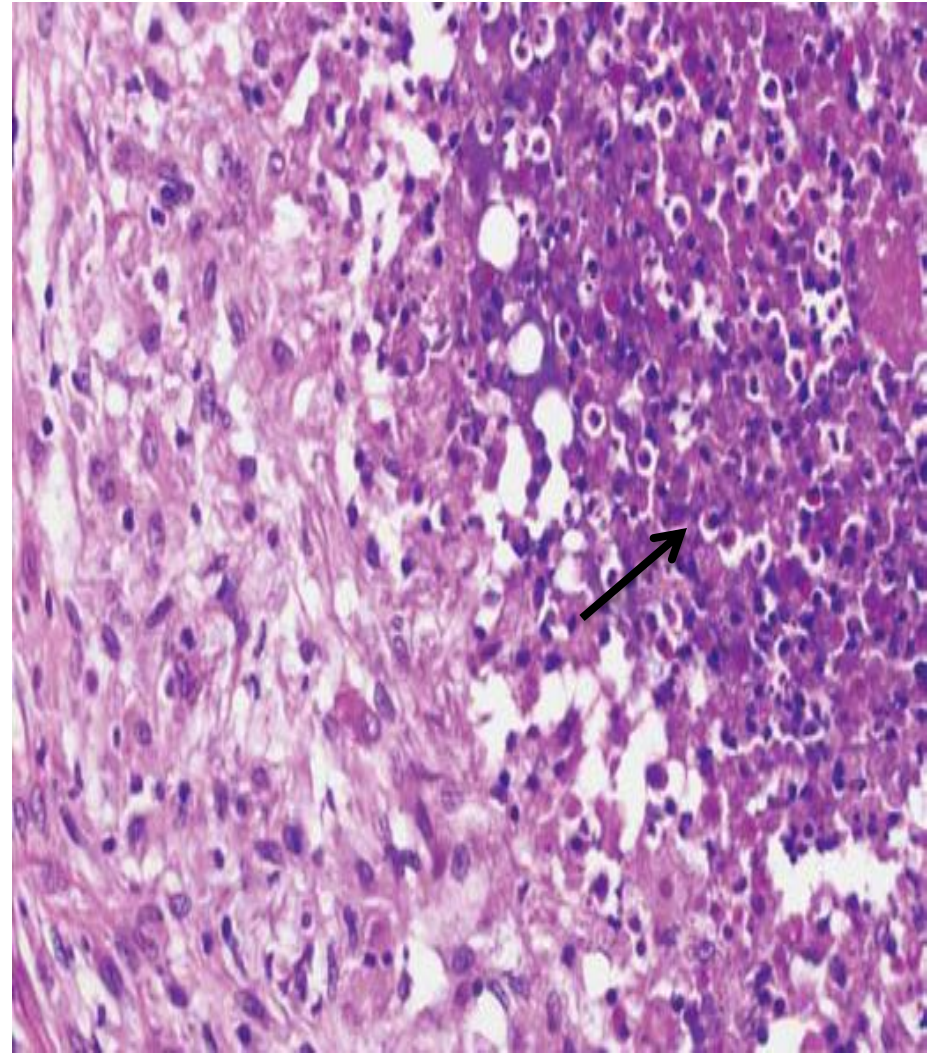
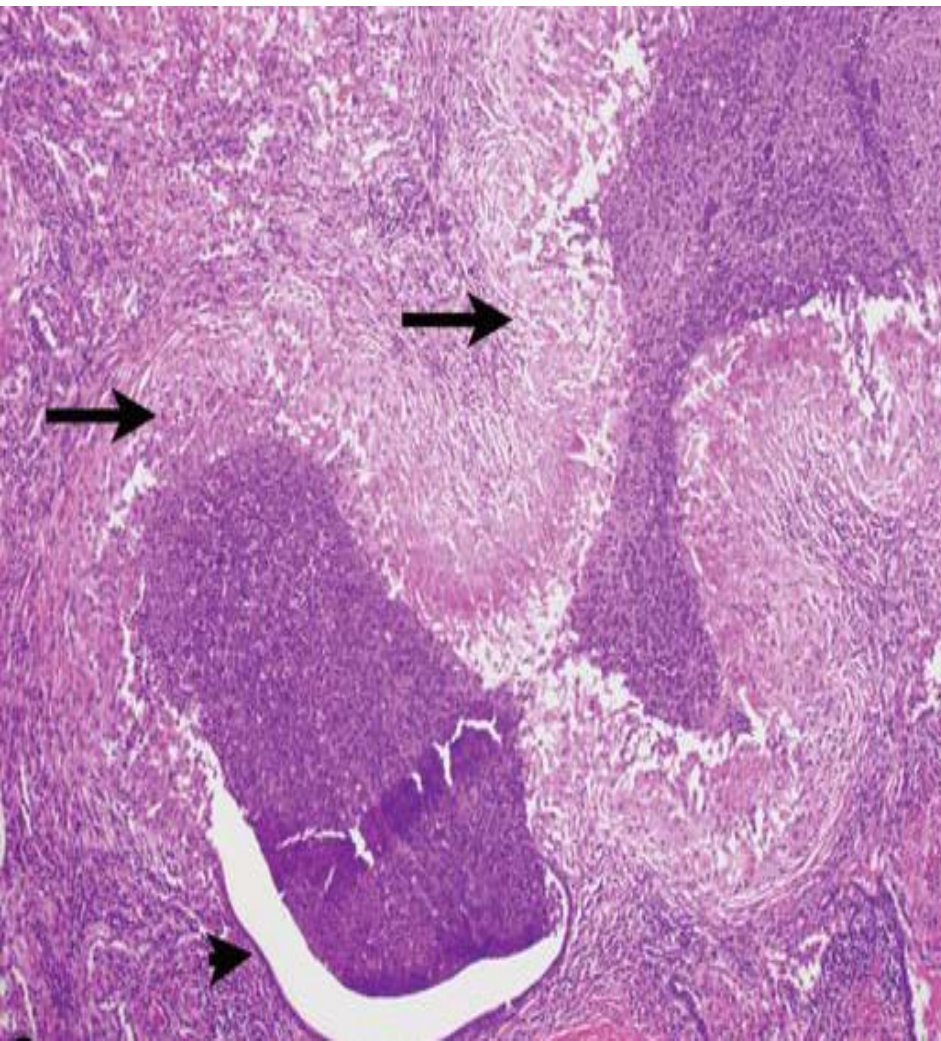


**Blastomyces: single thick walled yeasty within the giant cell and neutrophilic reaction. The single broad based bud of blastomyces is detected with silver stain.**



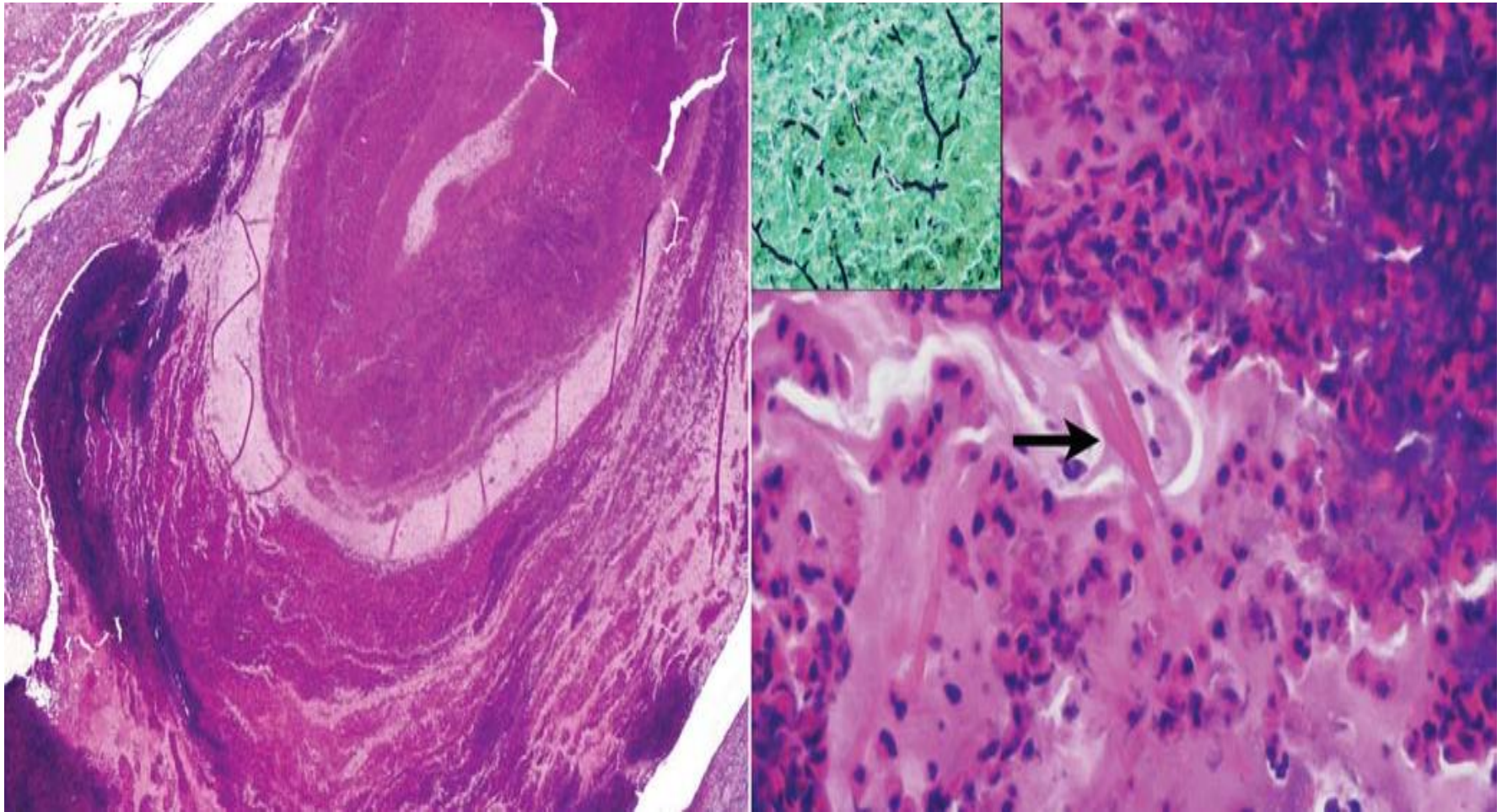


**Allergic bronchopulmonary Aspergillosis with necrotizing granuloma destroying a bronchiole. With abundant eosinophils in necrotic material (arrow)**





Allergic bronchopulmonary Aspergillosis with dilated bronchus filled with mucoid material, the branching hyphae are present within the mucus with abundant eosinophils



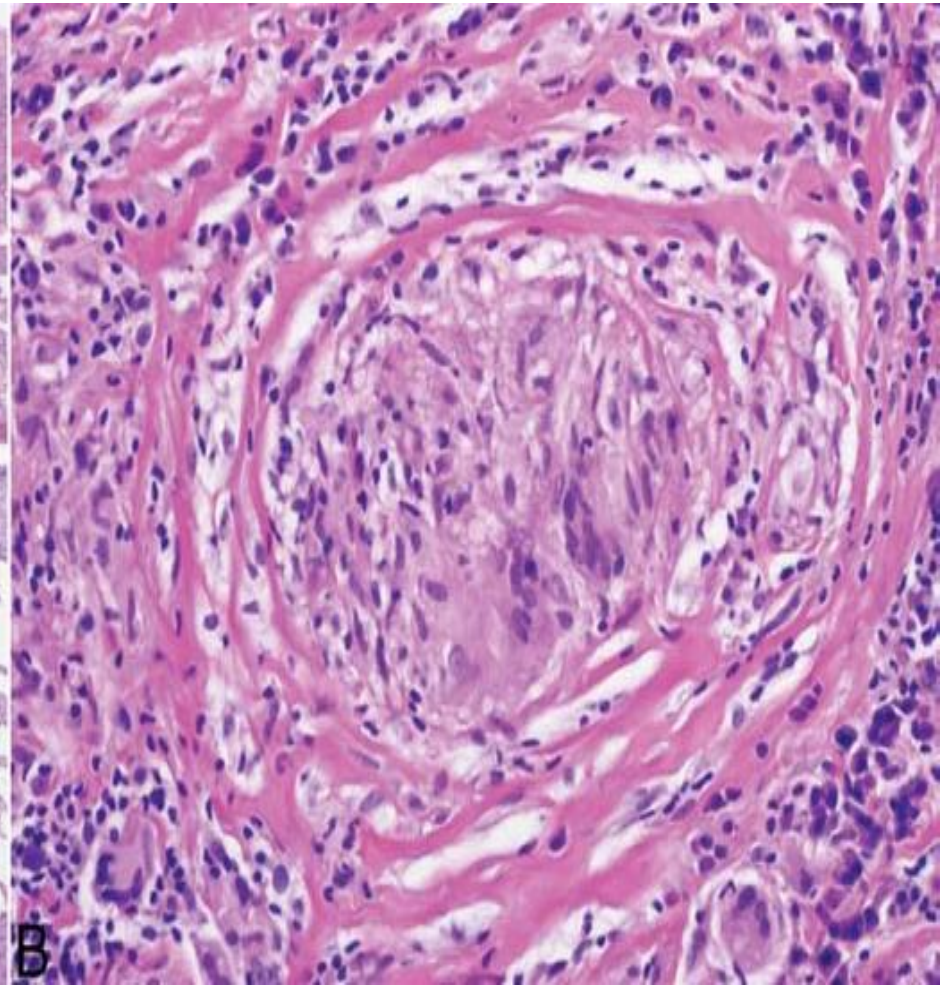
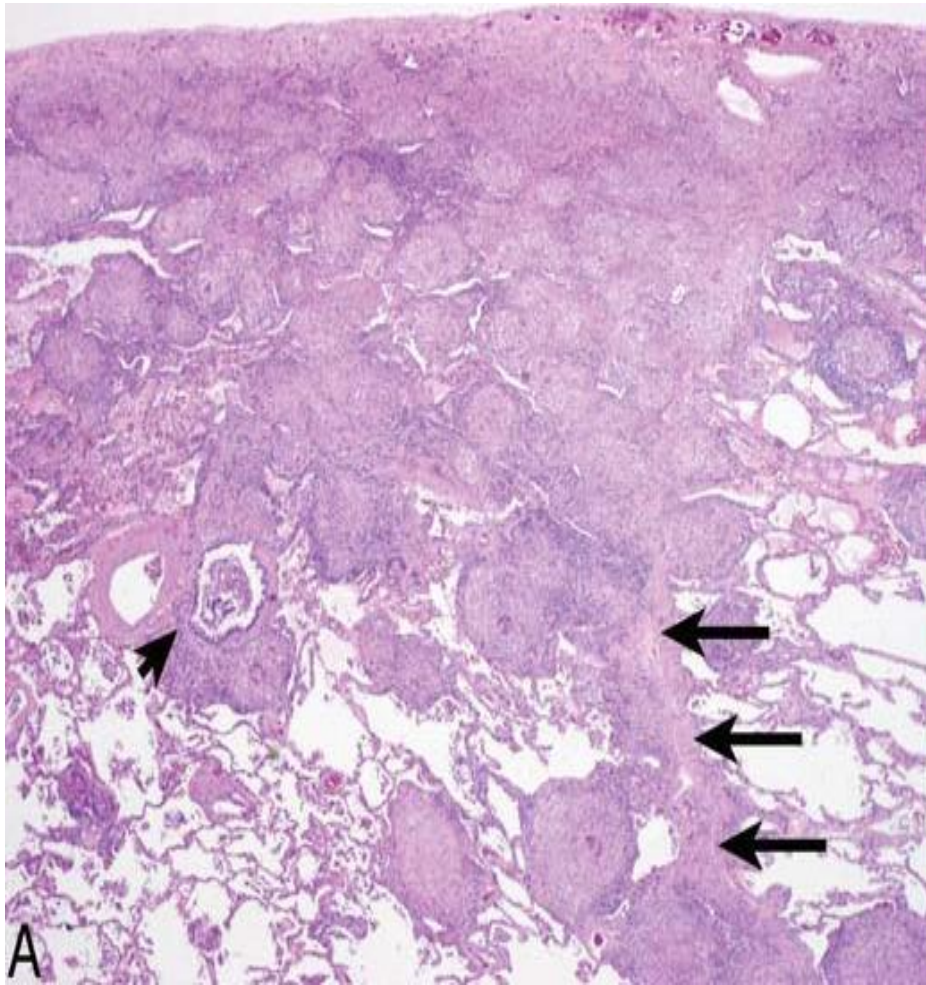
**Step 2: look for histological features  
of non infectious granulomatous  
inflammation**

**The main role of pathologist is to identify features not consistent with sarcoidosis and to exclude presence of organisms**

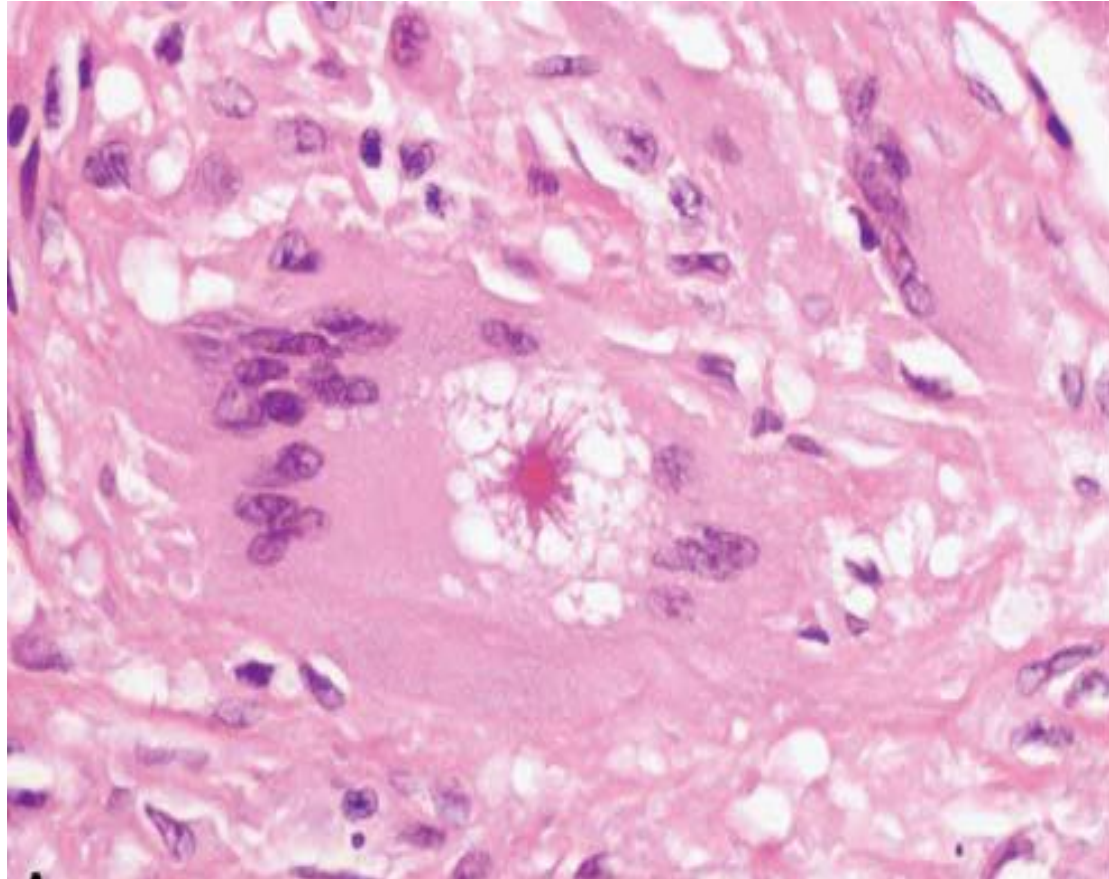
# Sarcoidosis



**prominent small well formed discrete non necrotizing granuloma in pleura, interlobular septa and walls of bronchioles with normal lung away from granuloma is seen in sarcoidosis**



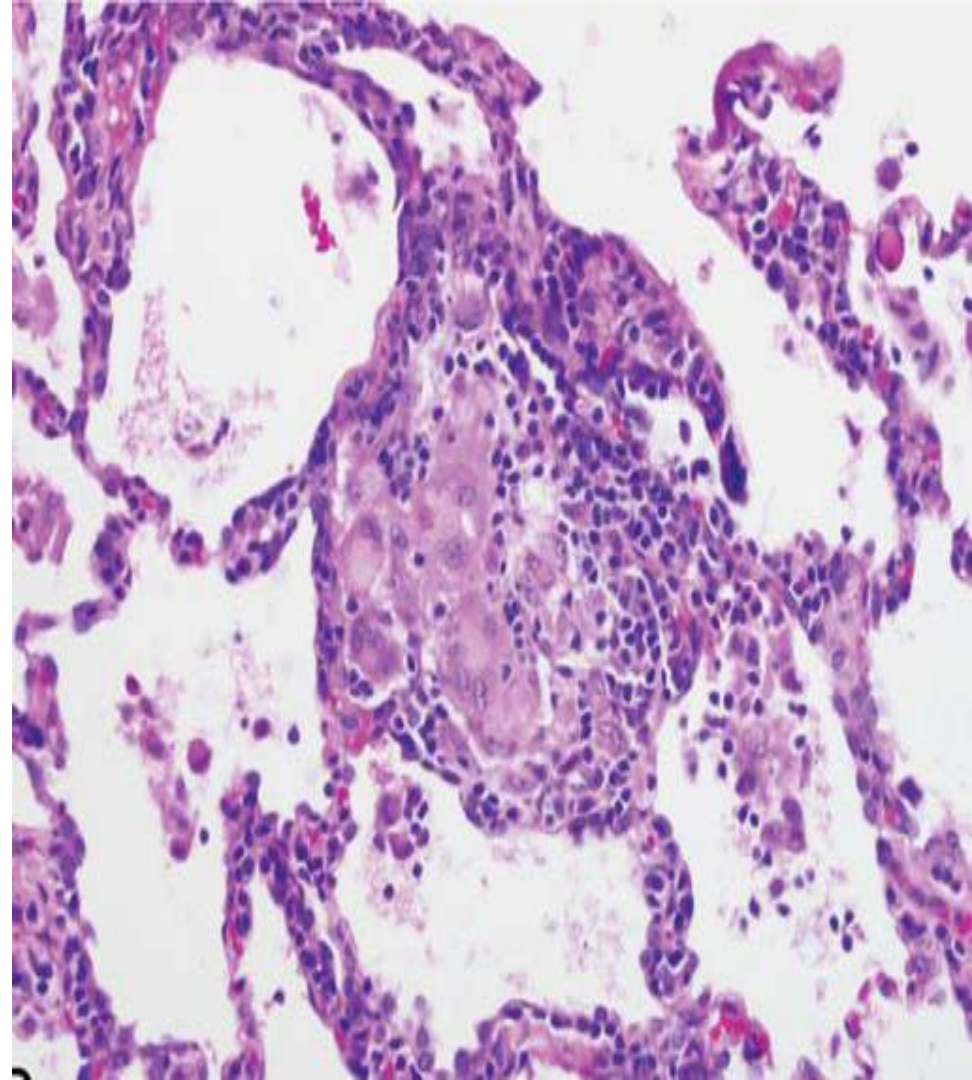
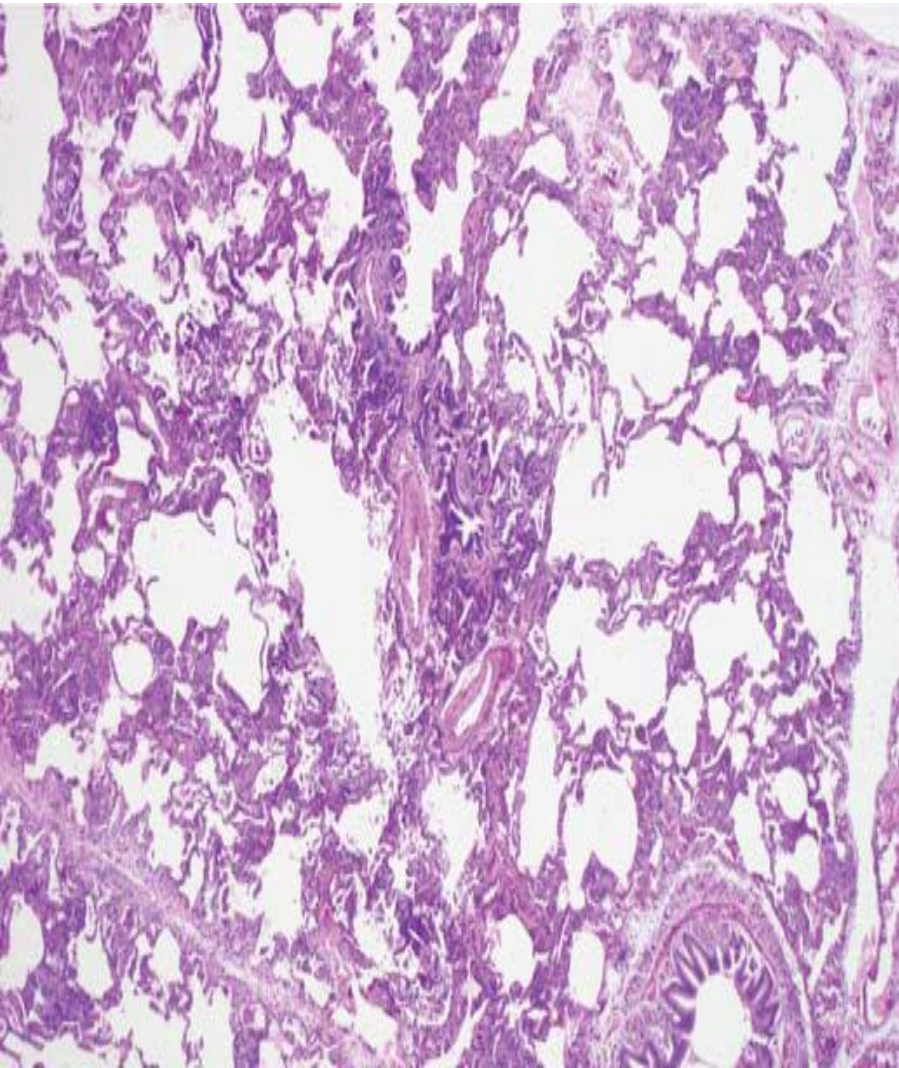
# Pink spider-like structures (Asteroid body) in sarcoidosis



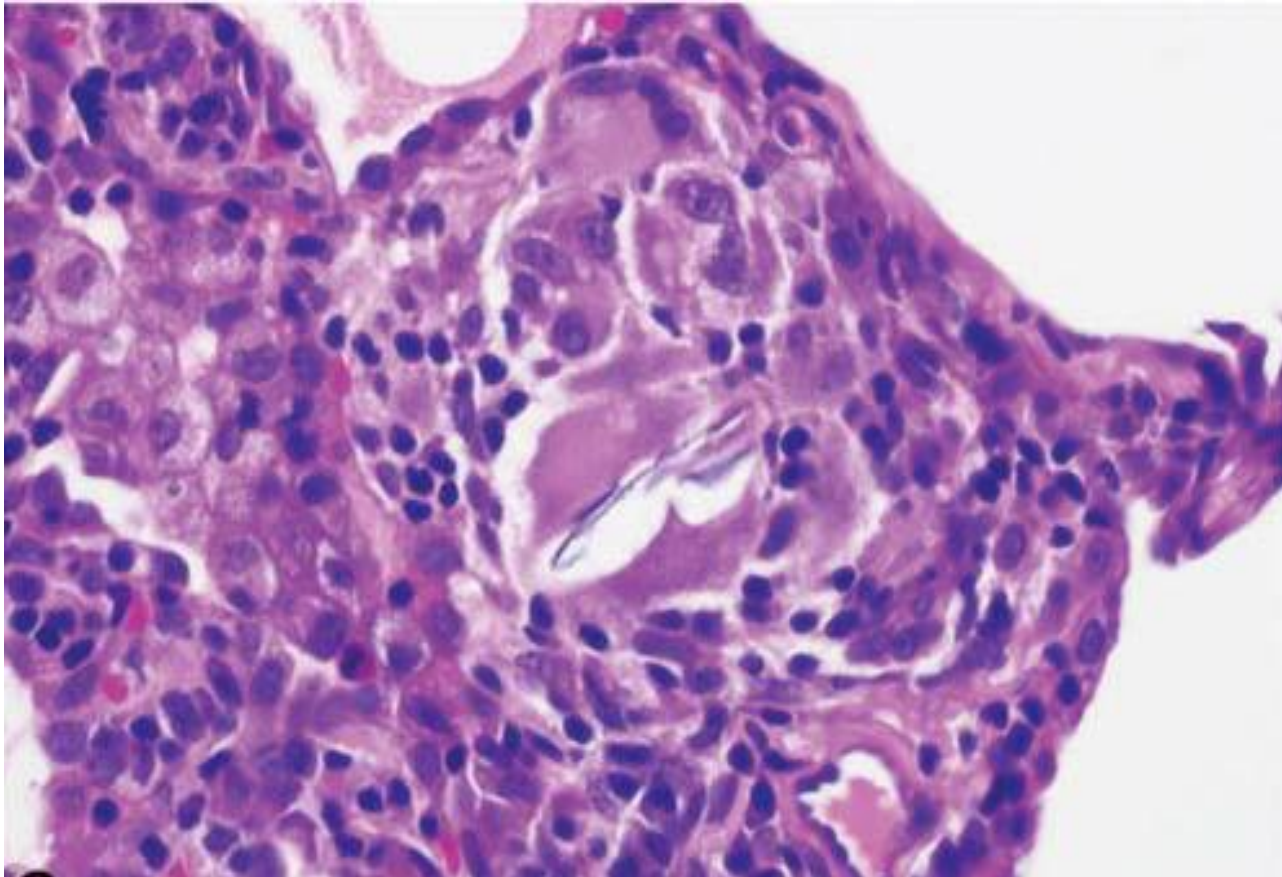
# **Hypersensitivity pneumonitis**



Prominent interstitial chronic inflammation with scattered **small poorly formed granulomas** or only multinucleated giant cells in interstitium is seen in hypersensitivity pneumonitis

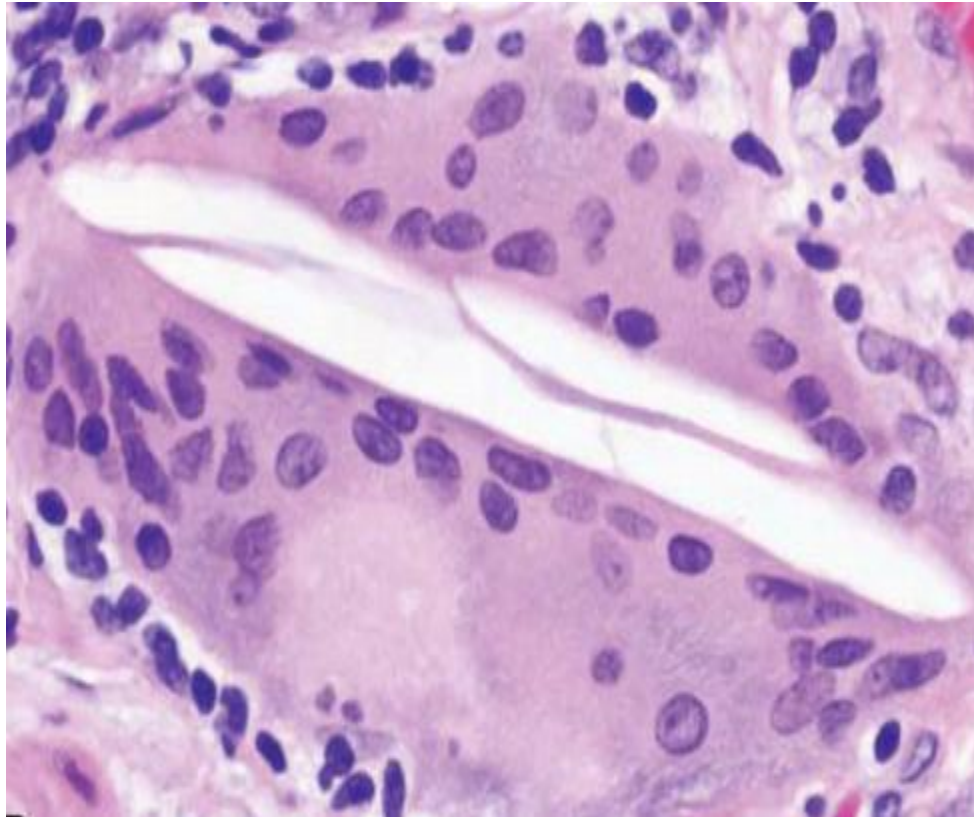


Needle shaped crystalline inclusion  
(endogenous) in hypersensitivity  
pneumonitis



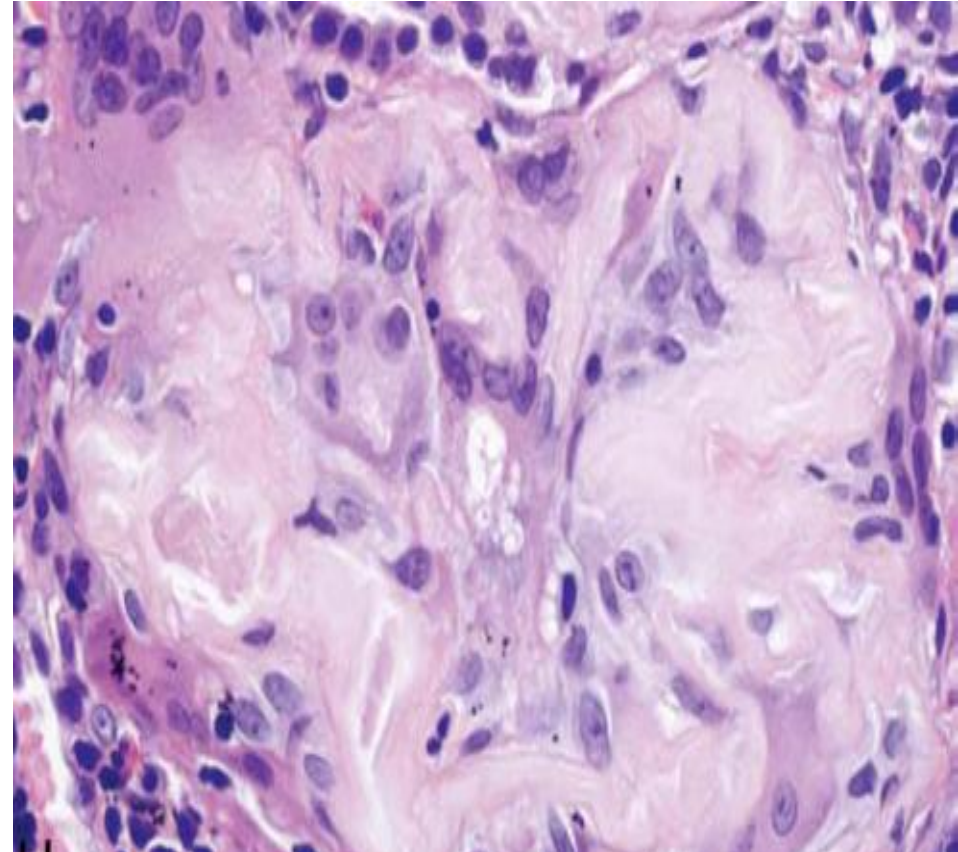
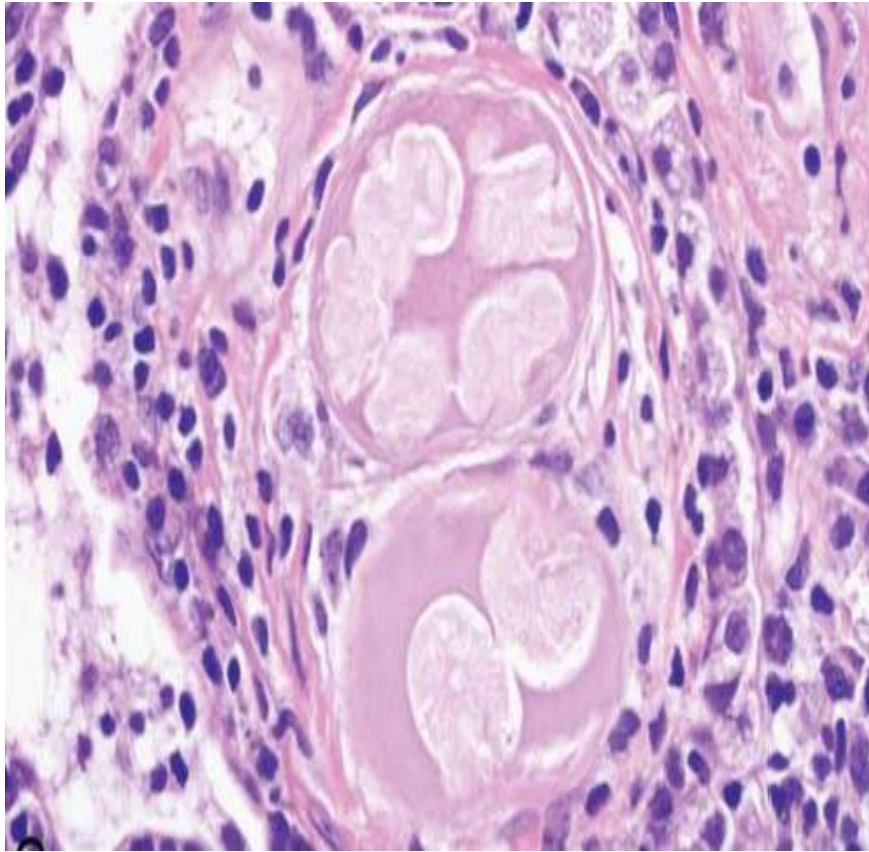


# Cholesterol cleft (endogenous) in hypersensitivity pneumonitis



# Aspiration pneumonia

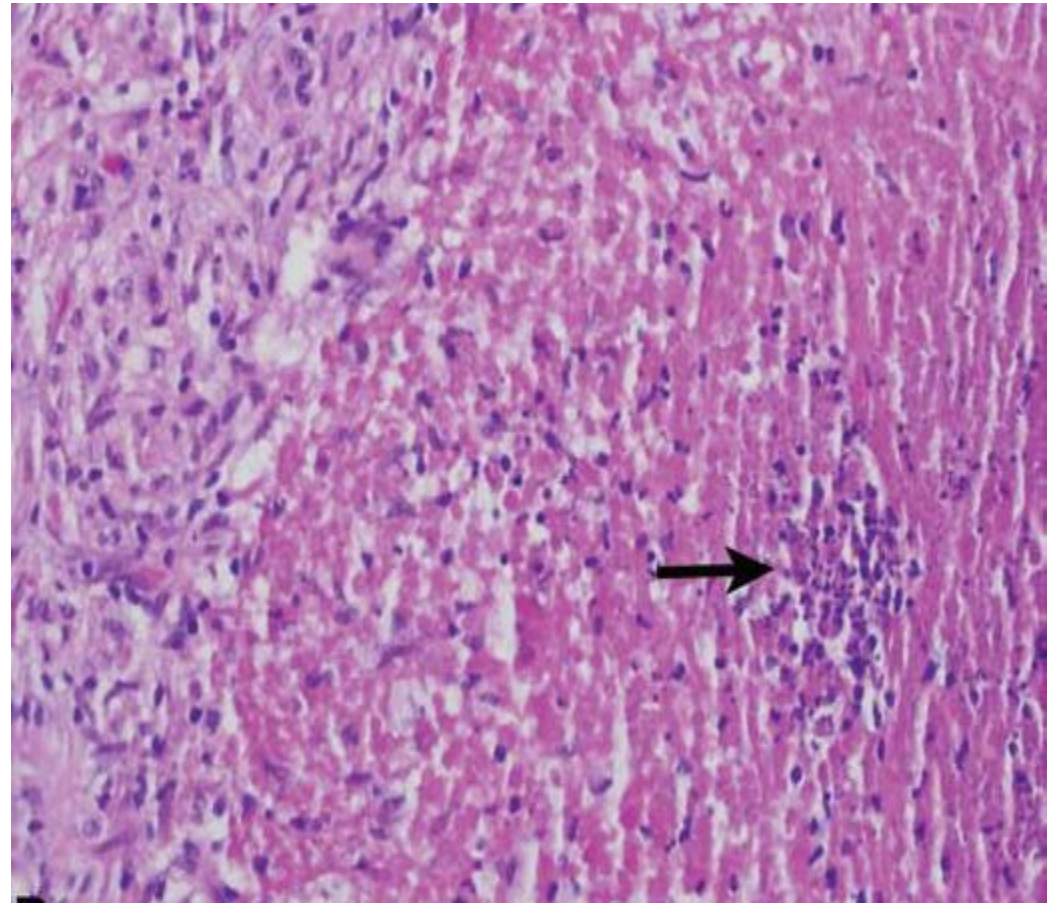
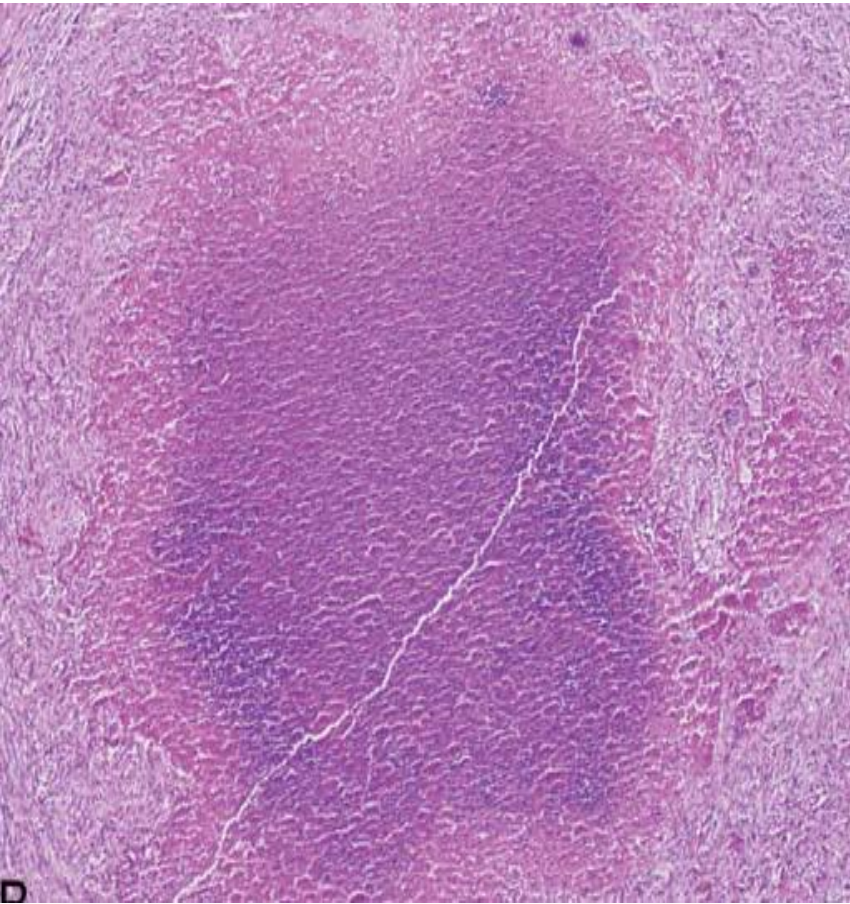
# Vegetable particles in aspiration pneumonia



# wegener granulomatosis

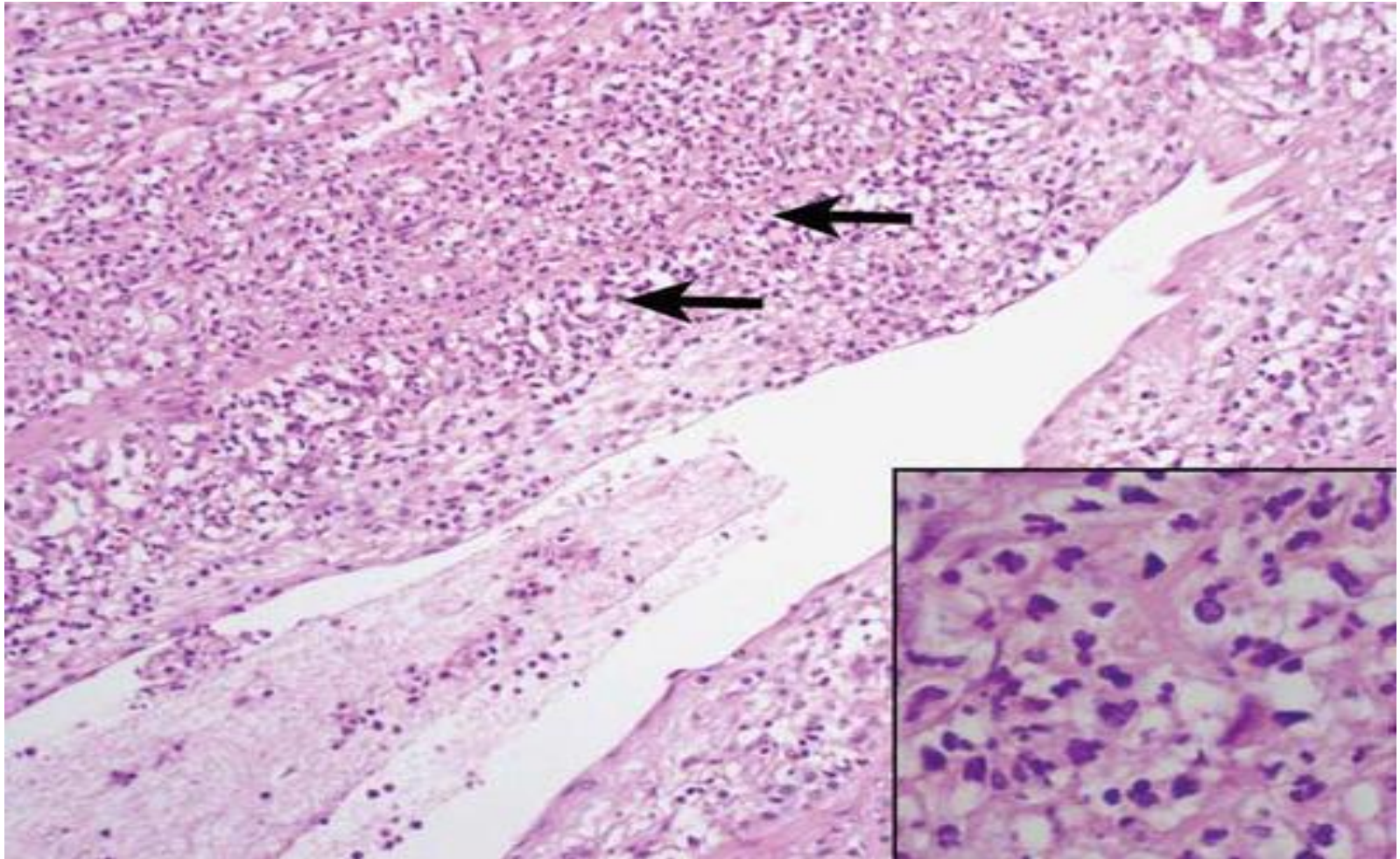


Wegener granulomatosis: necrotizing  
granuloma with **dirty** **suppurative**  
**necrosis**



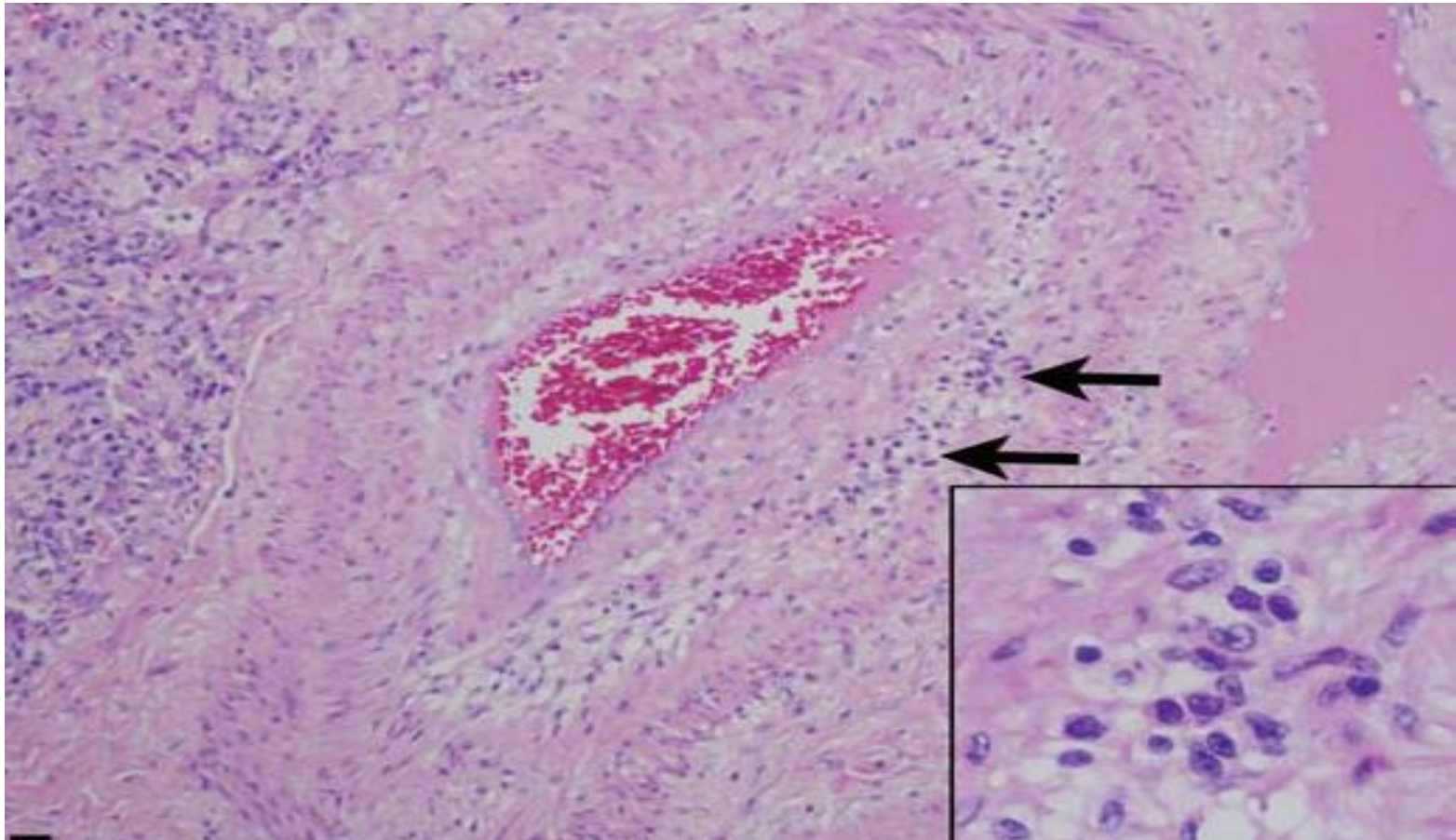


Vasculitis is an additional differentiating feature of Wegener granulomatosis, the predominant cellular infiltrate is neutrophil





While the main inflammatory infiltrate that accompany the vasculitis of mycobacterial infection are lymphocytes



**Thank you**